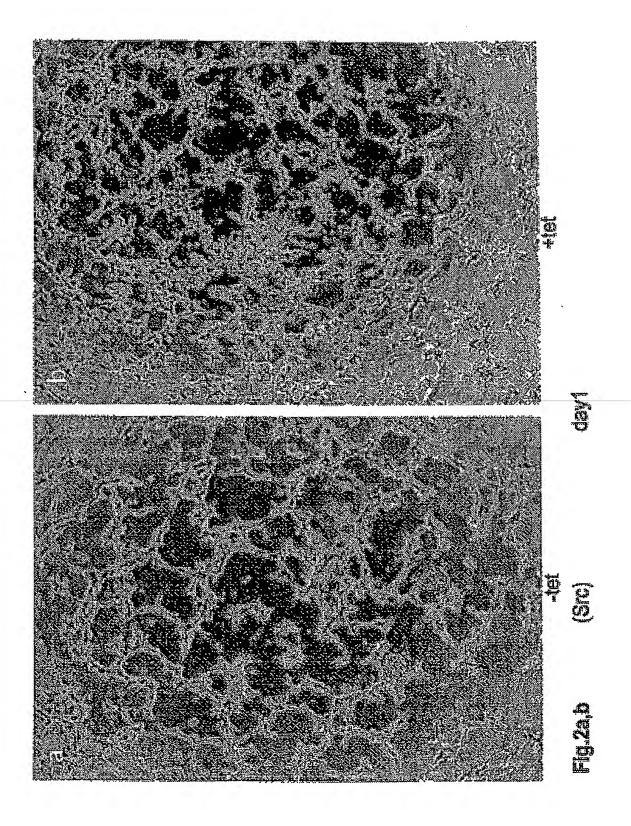
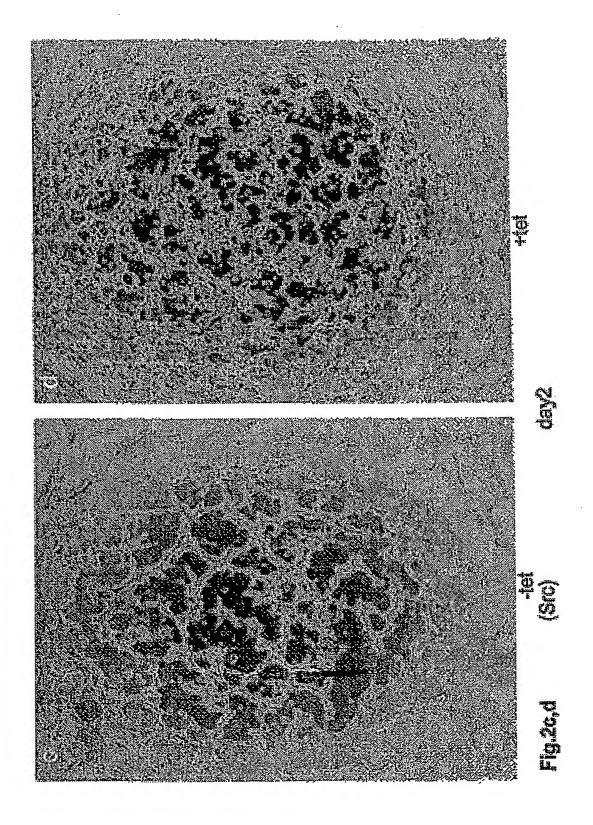
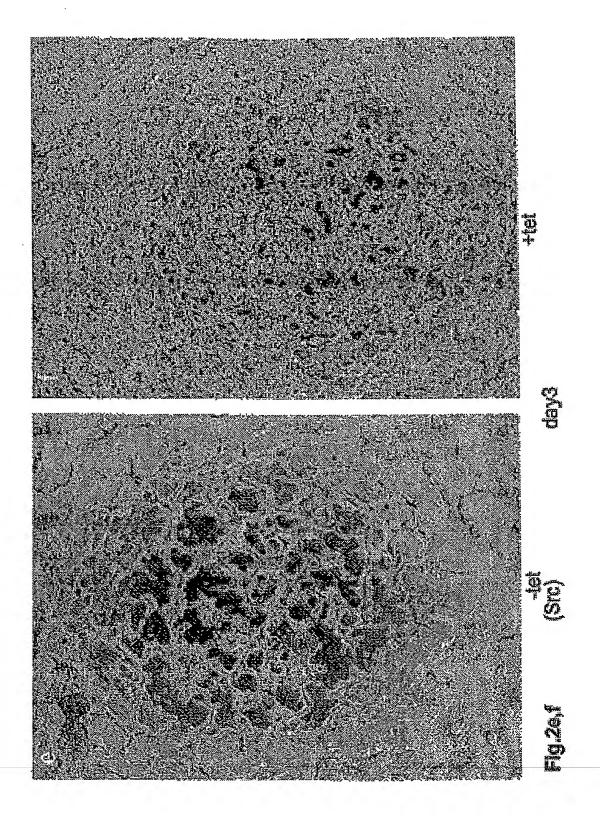
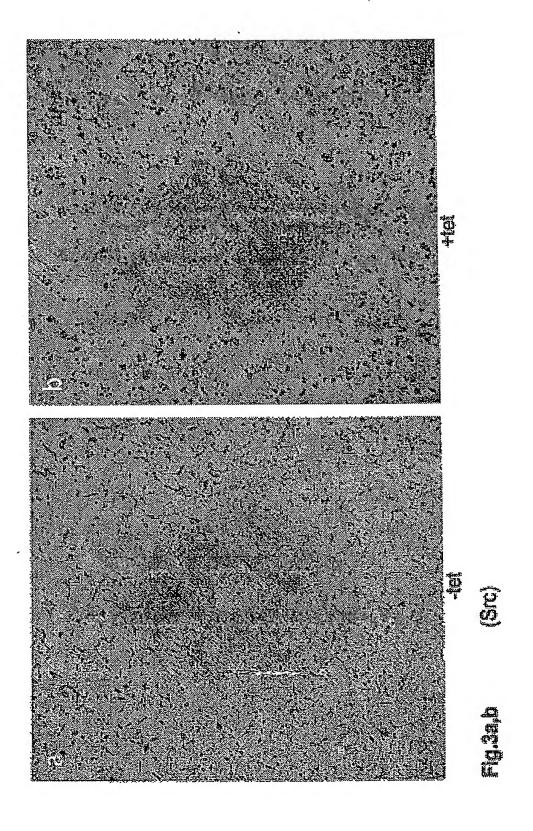


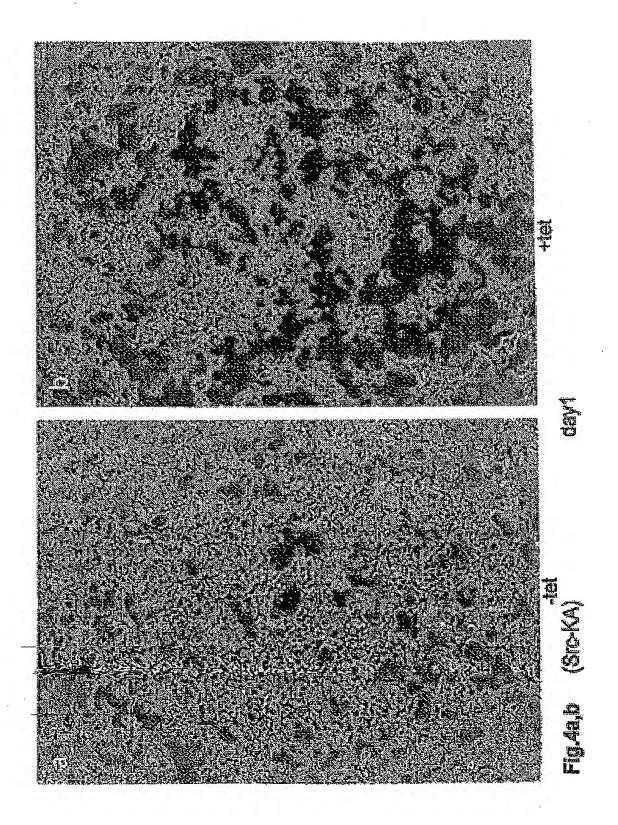
Fig. 1

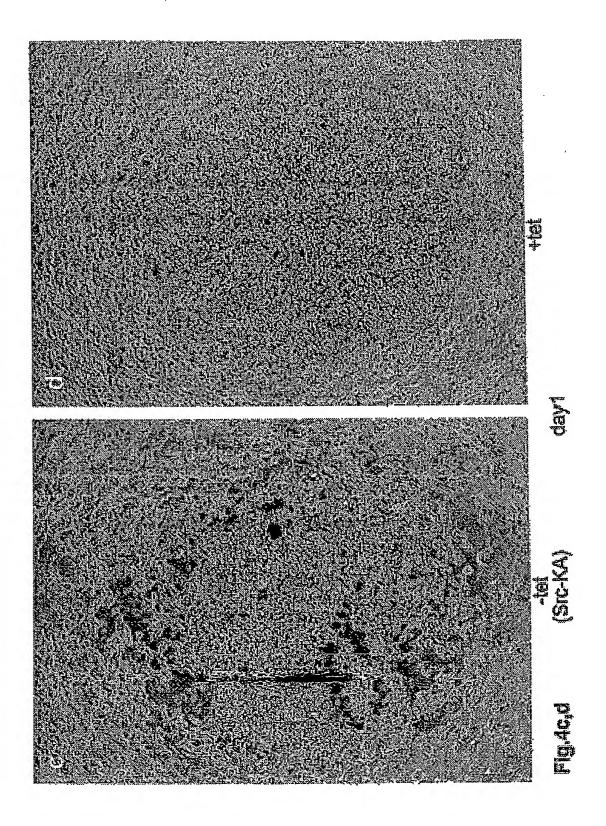


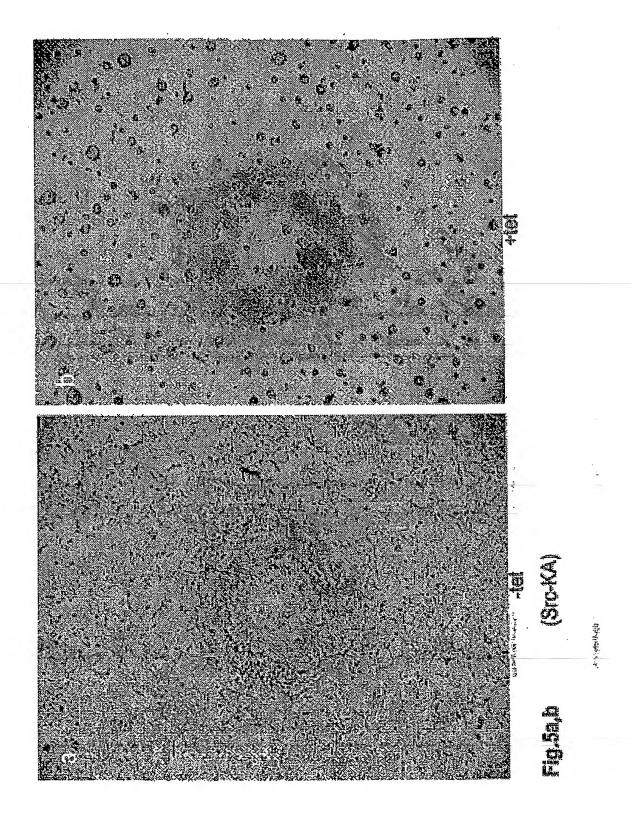


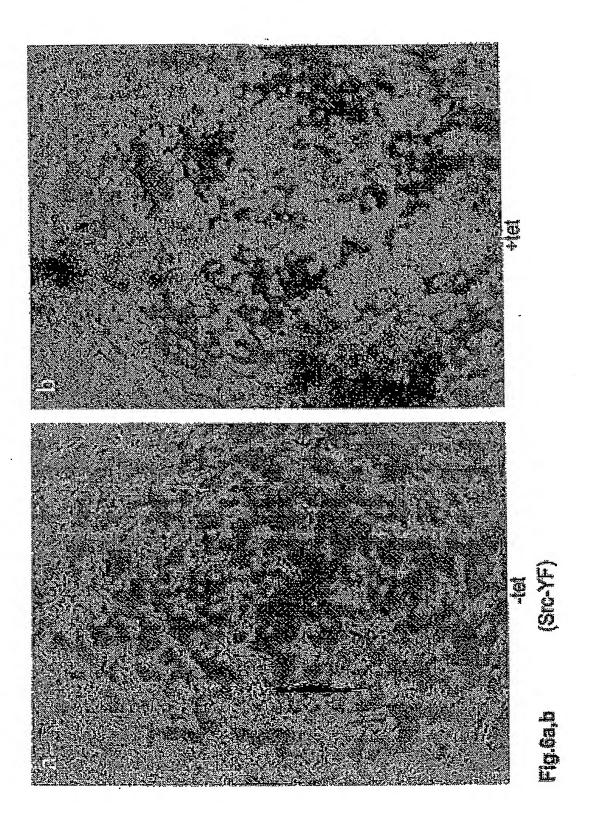


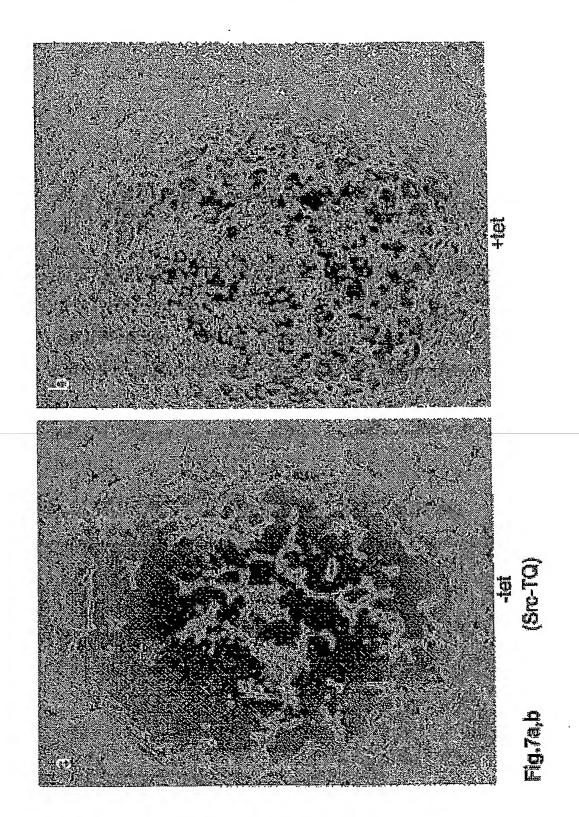


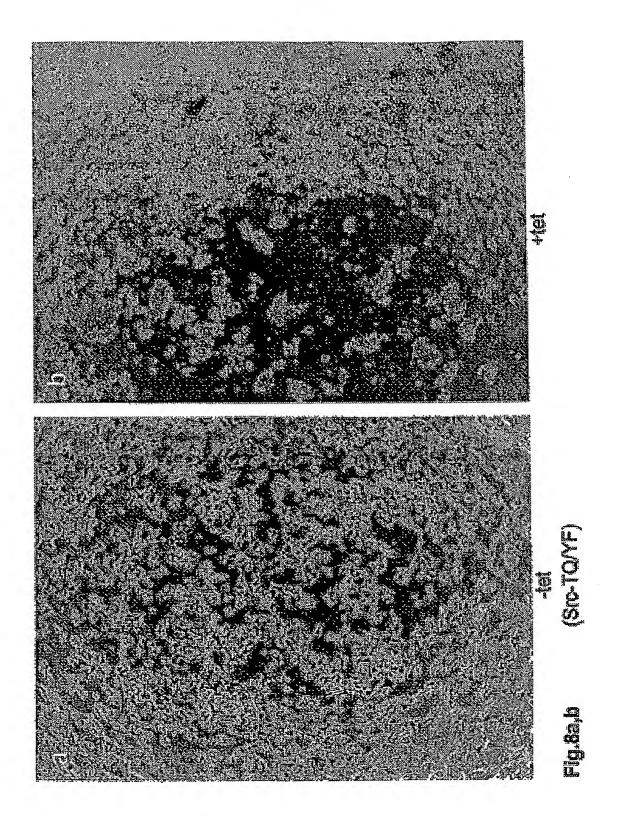


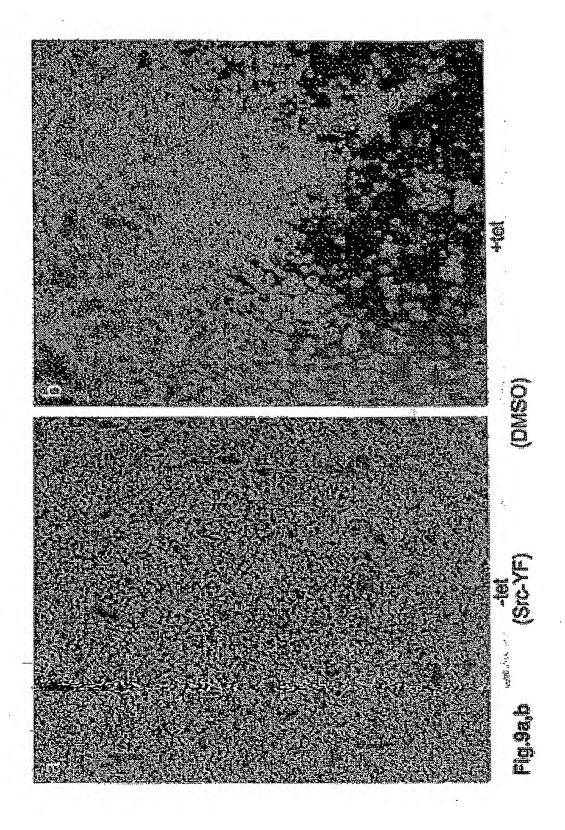


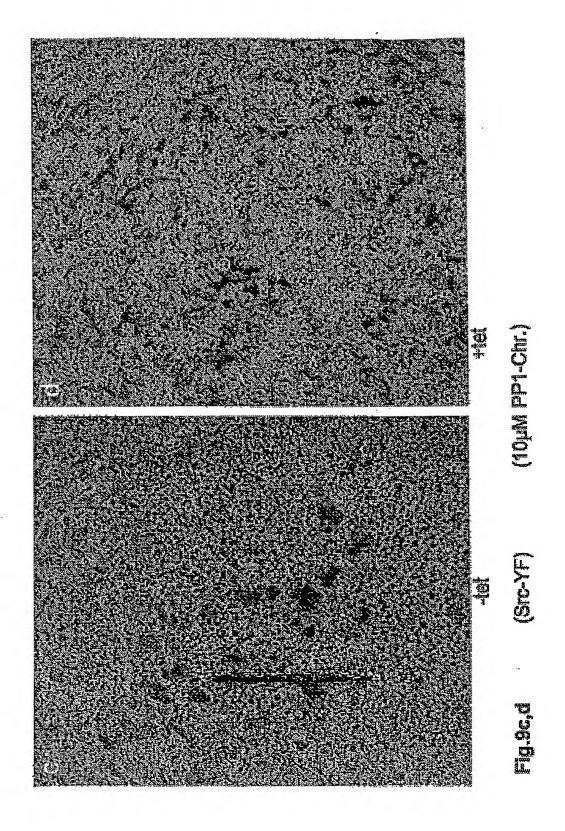


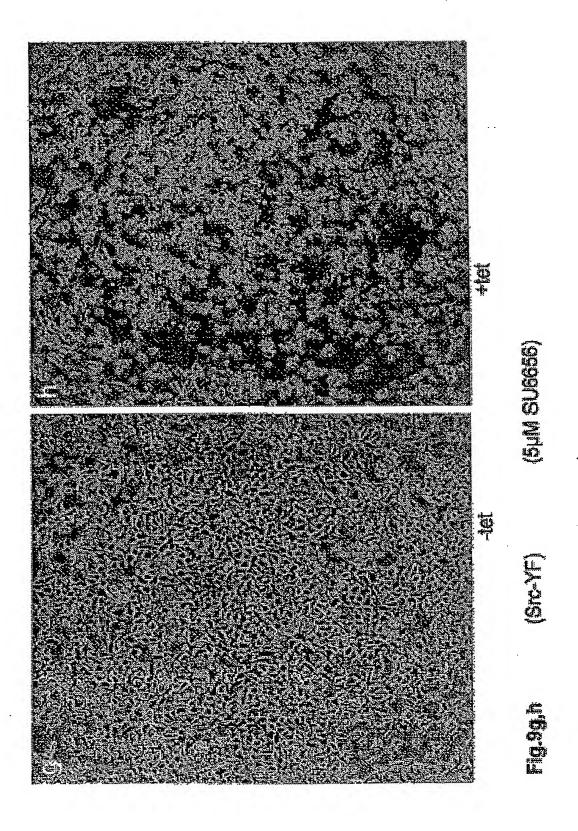


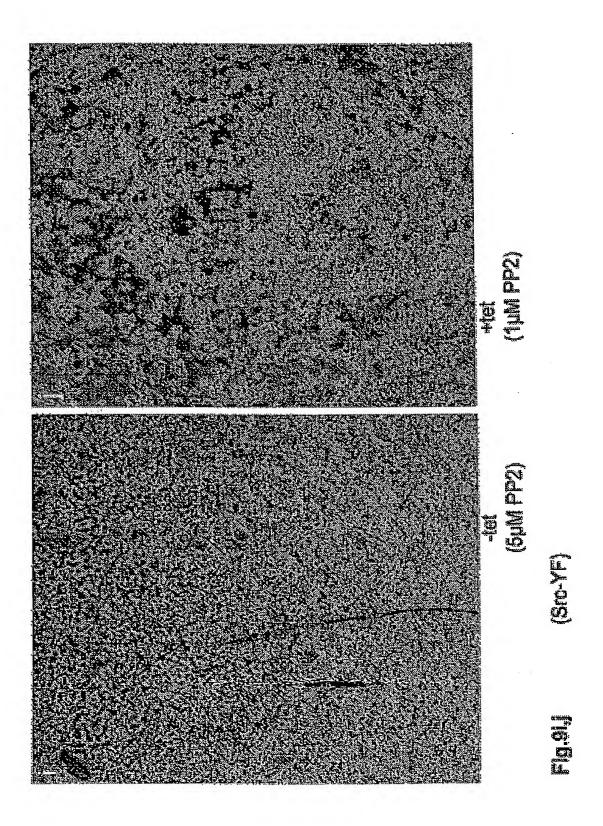


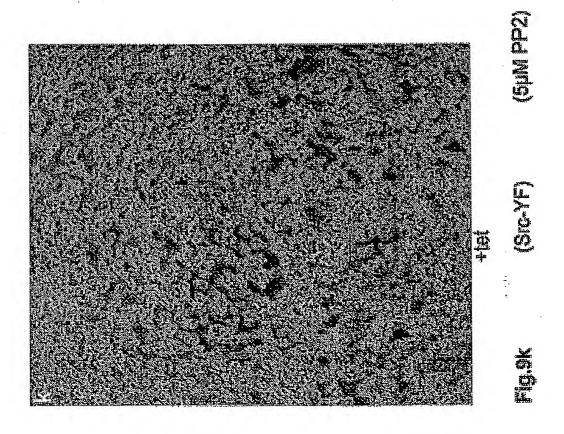


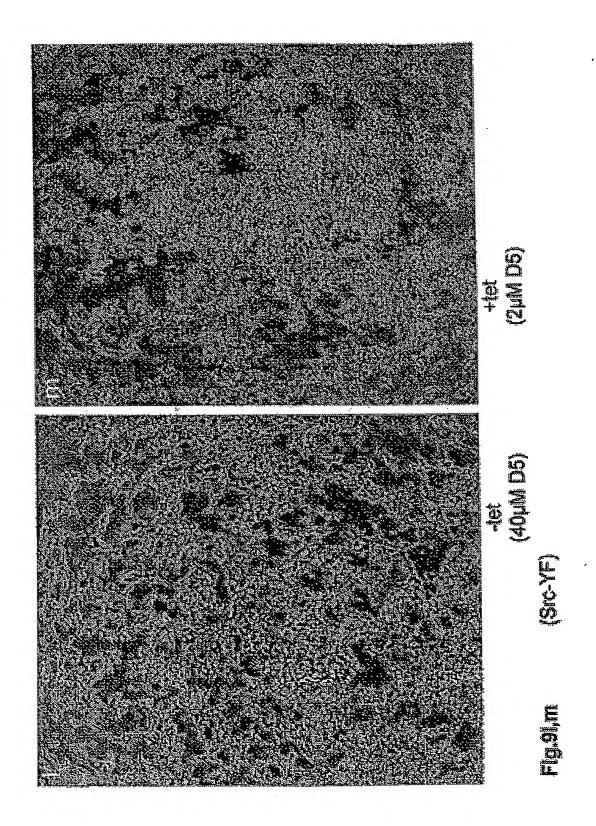


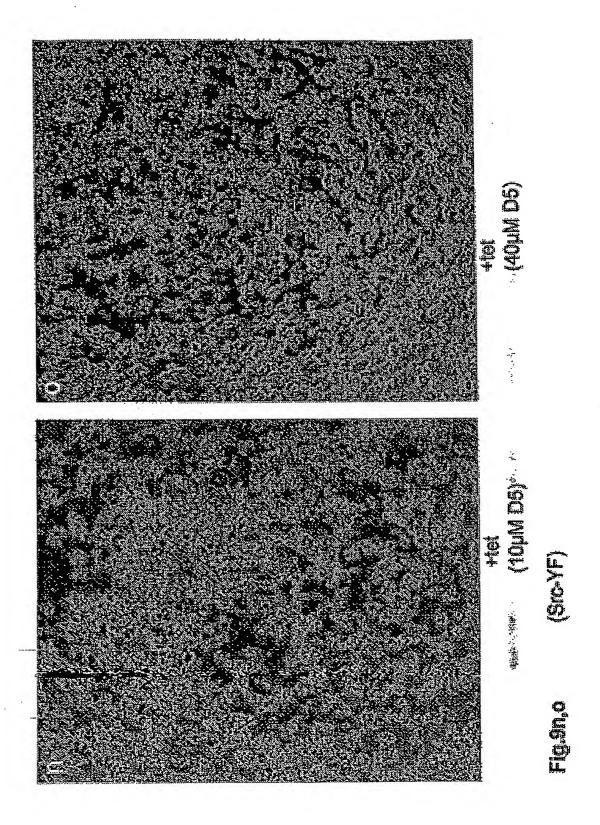








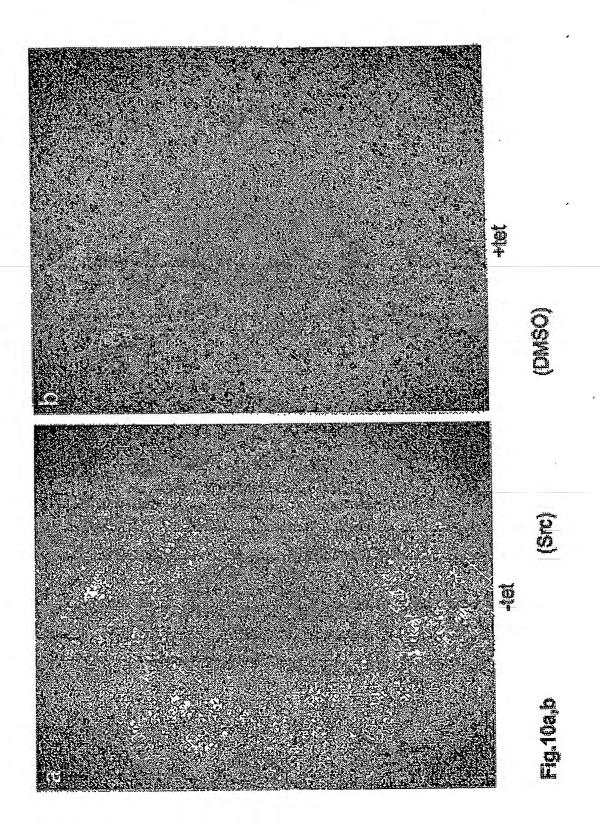


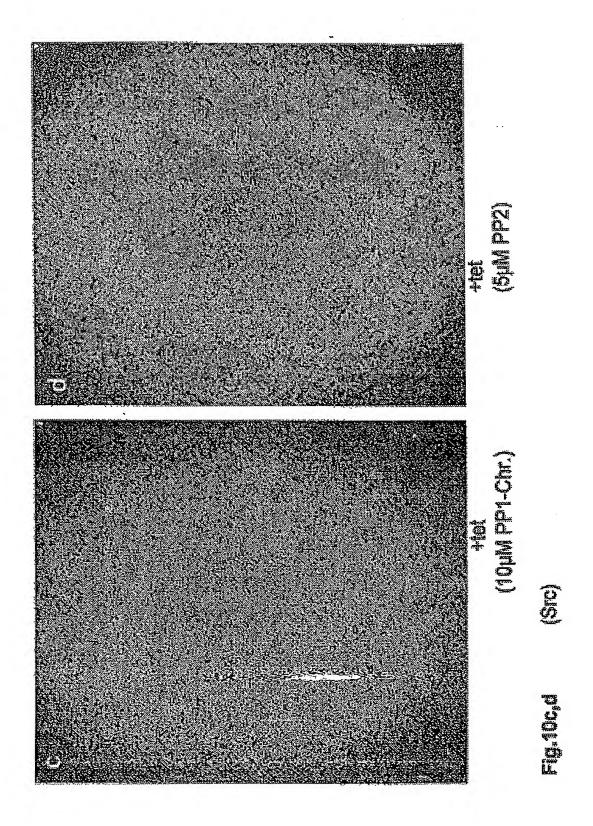


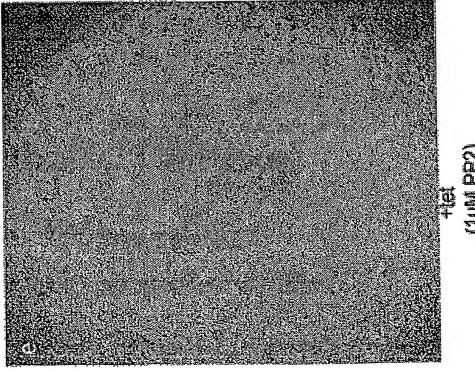
). 131

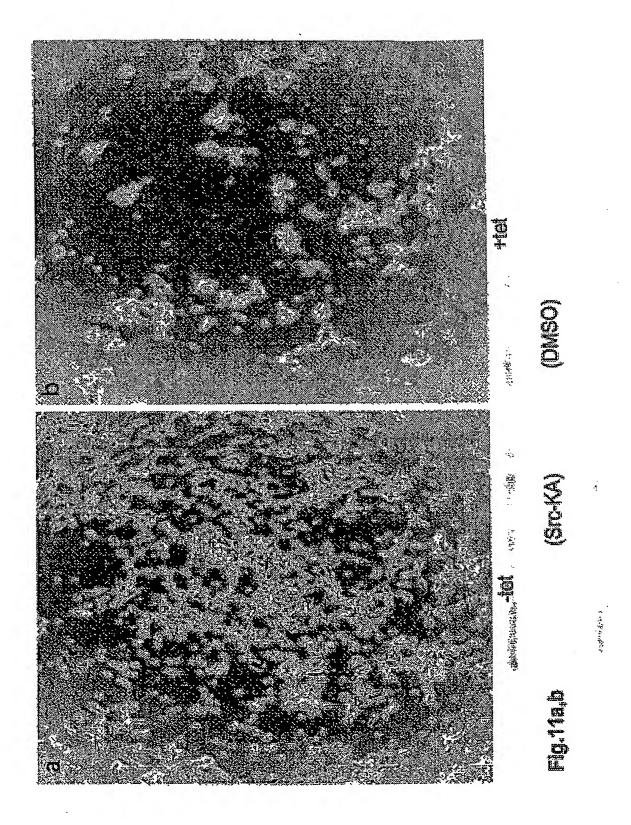
1000

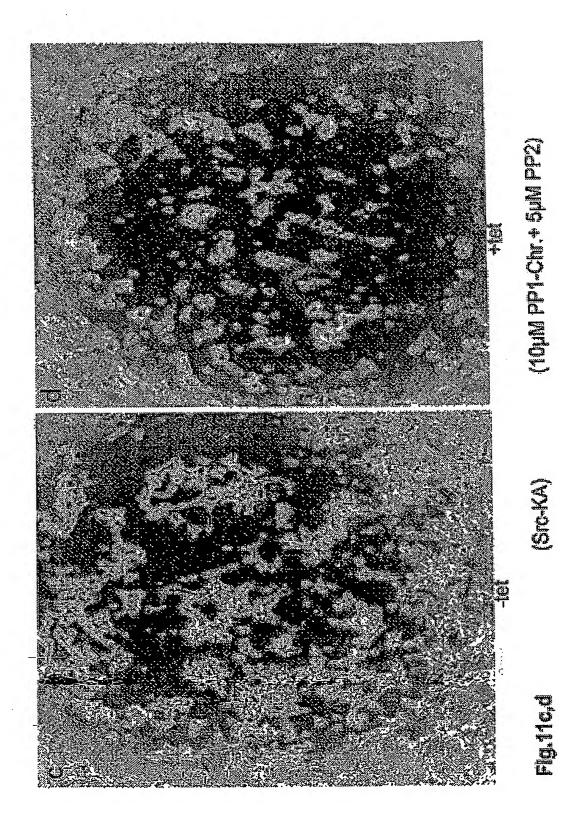
whiteway problems



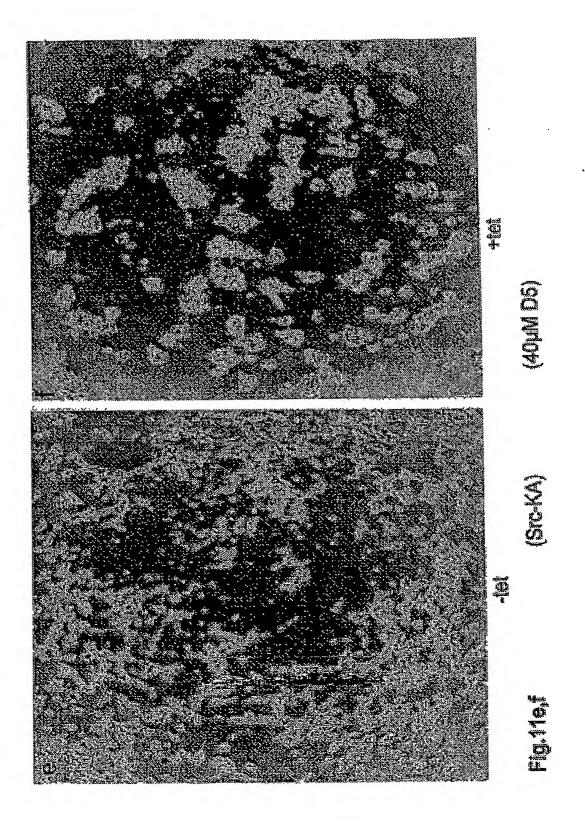


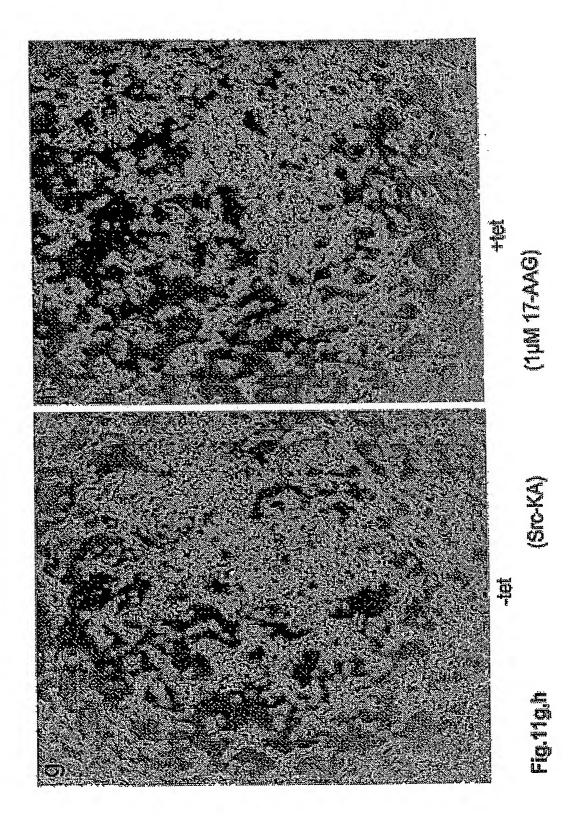


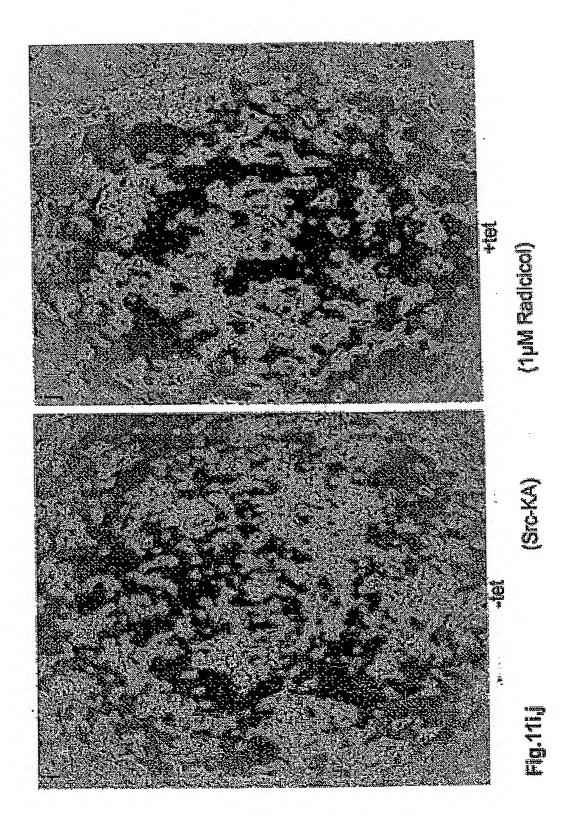


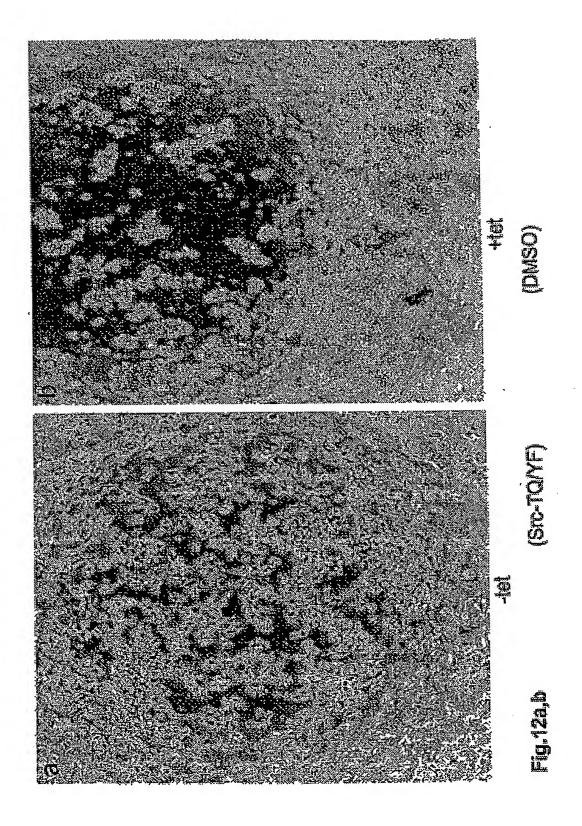


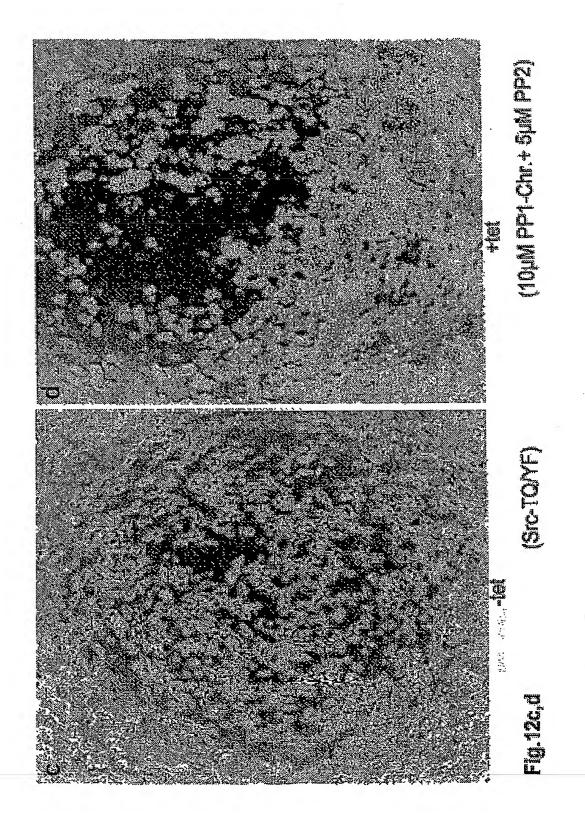
· ;

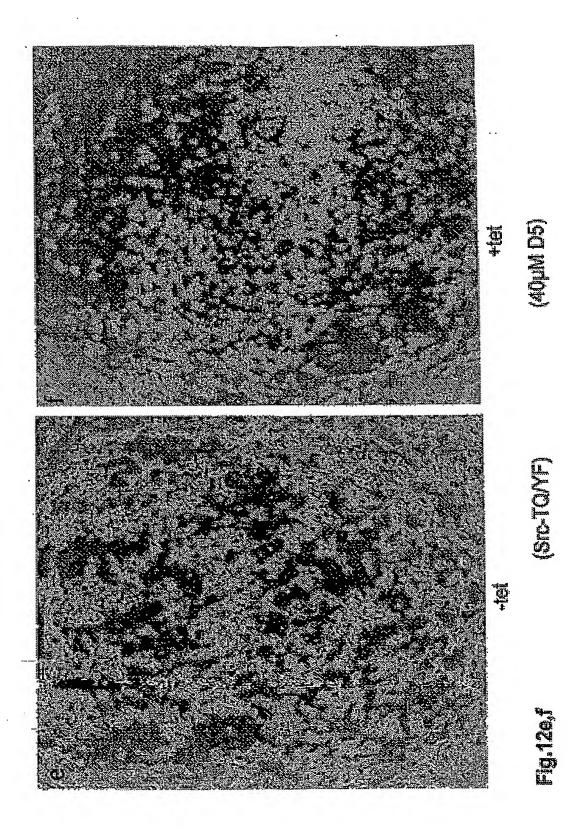


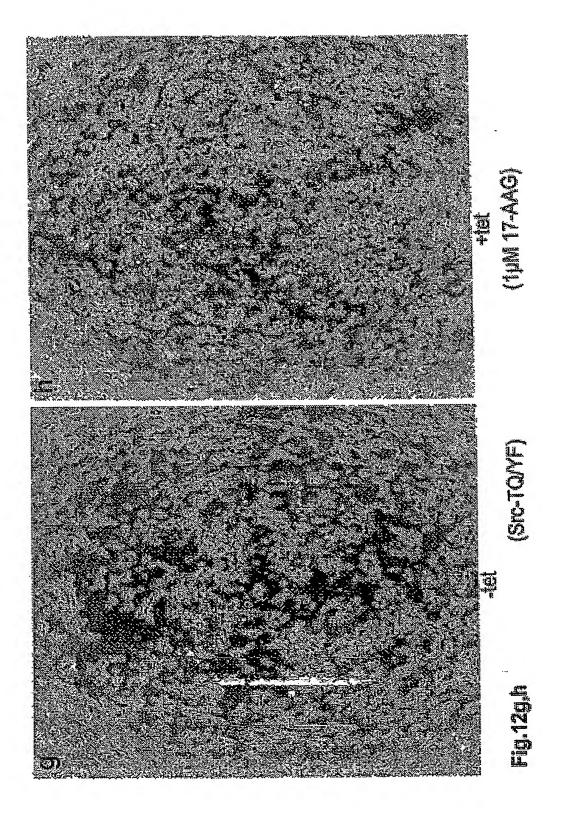


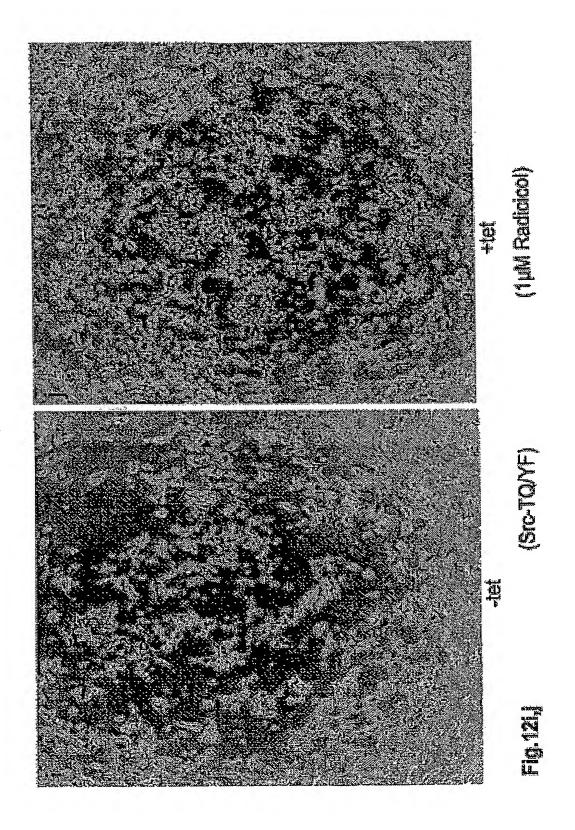


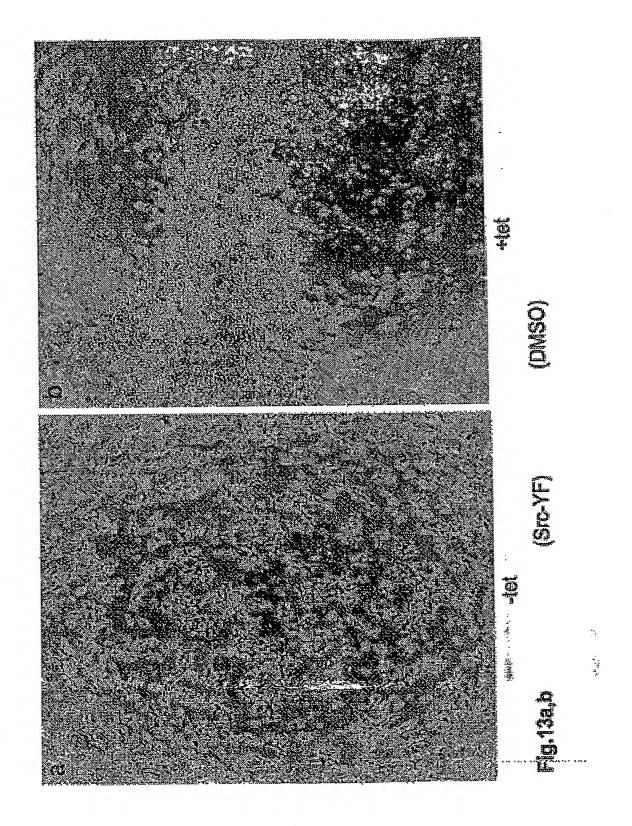


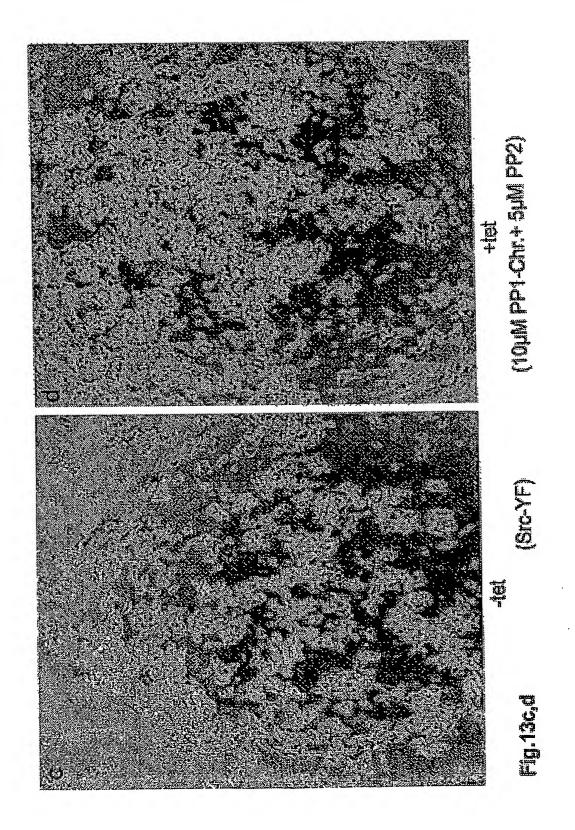


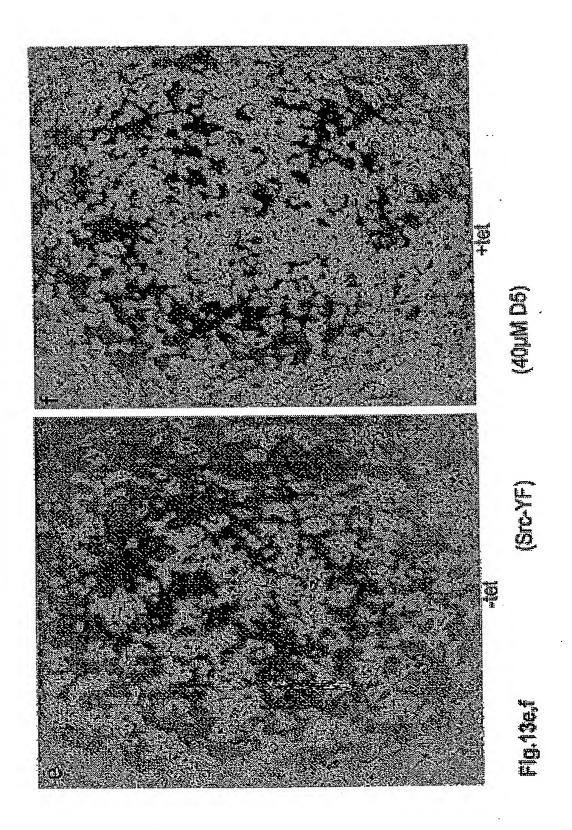


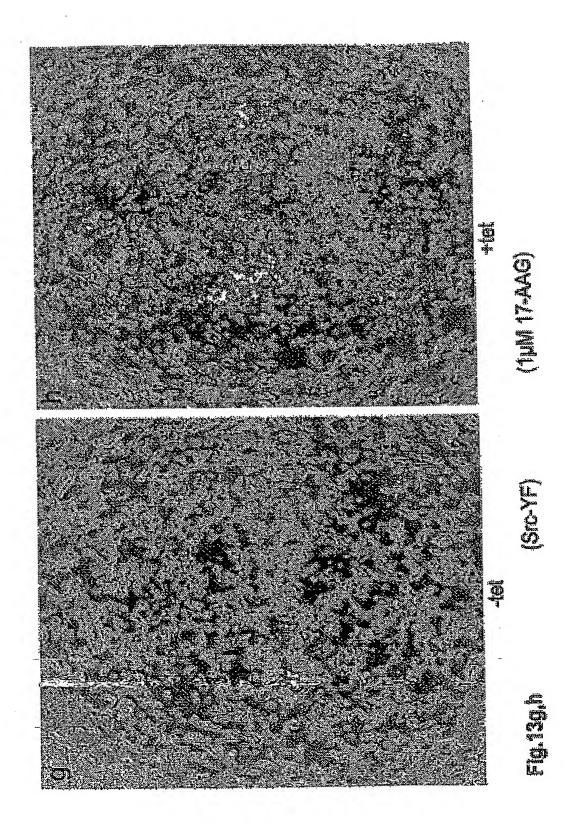


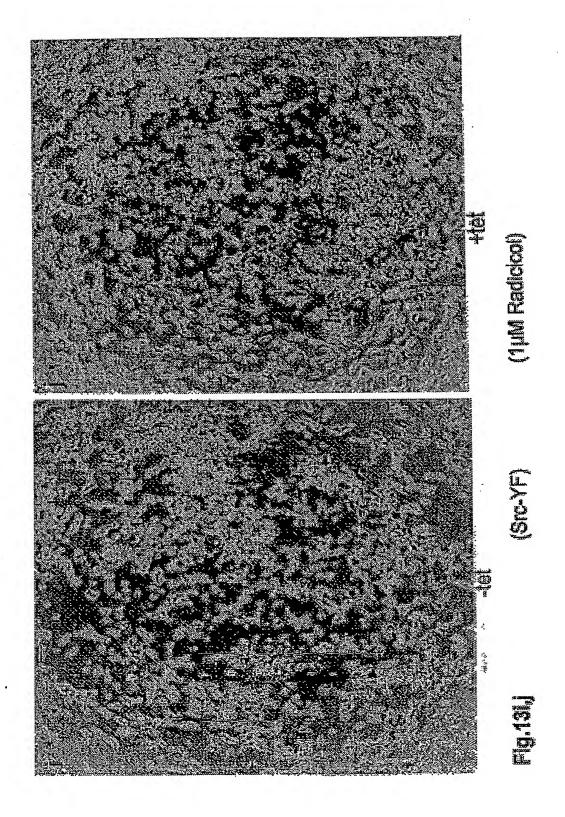


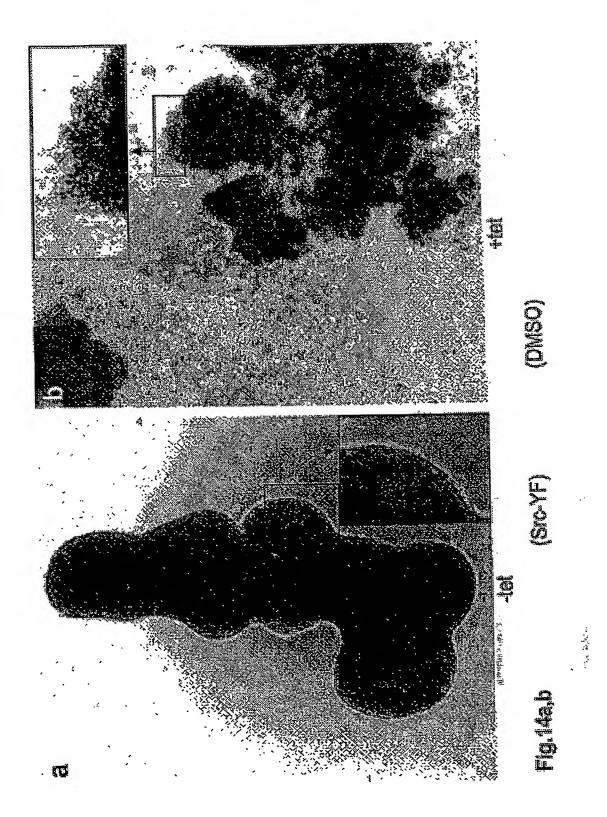


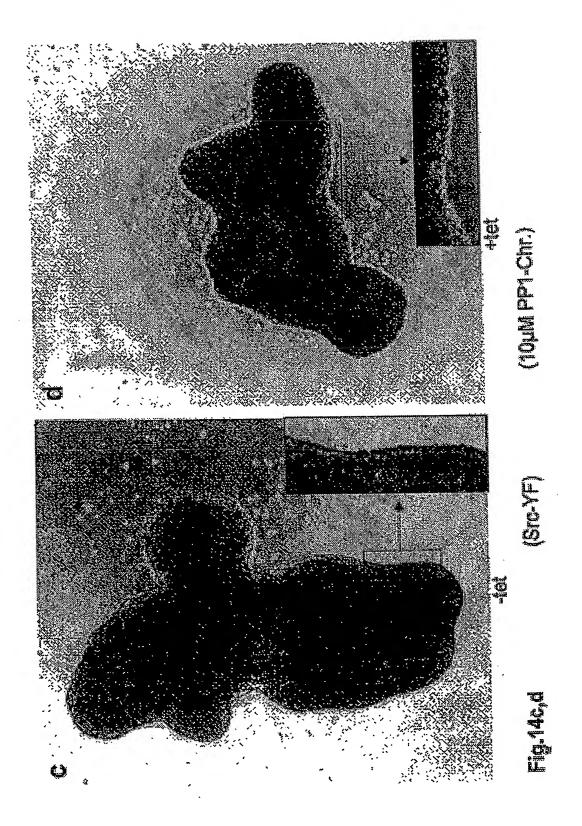


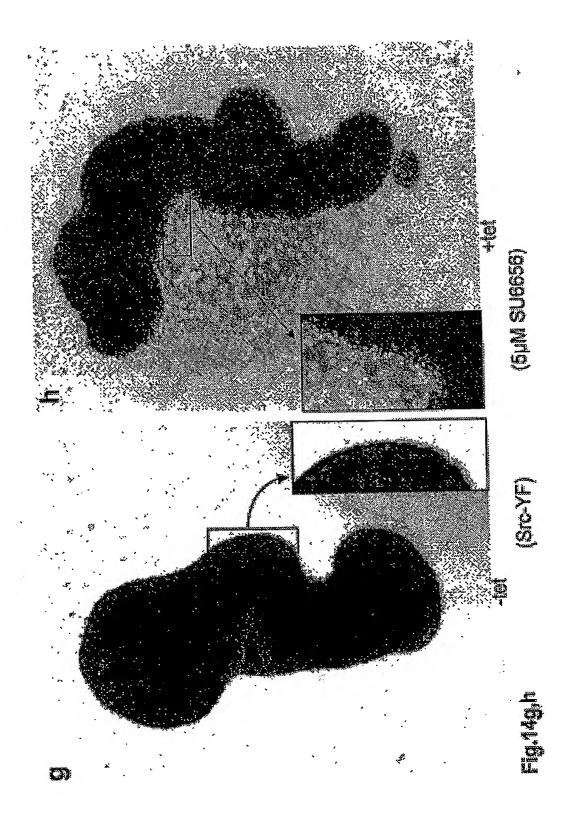


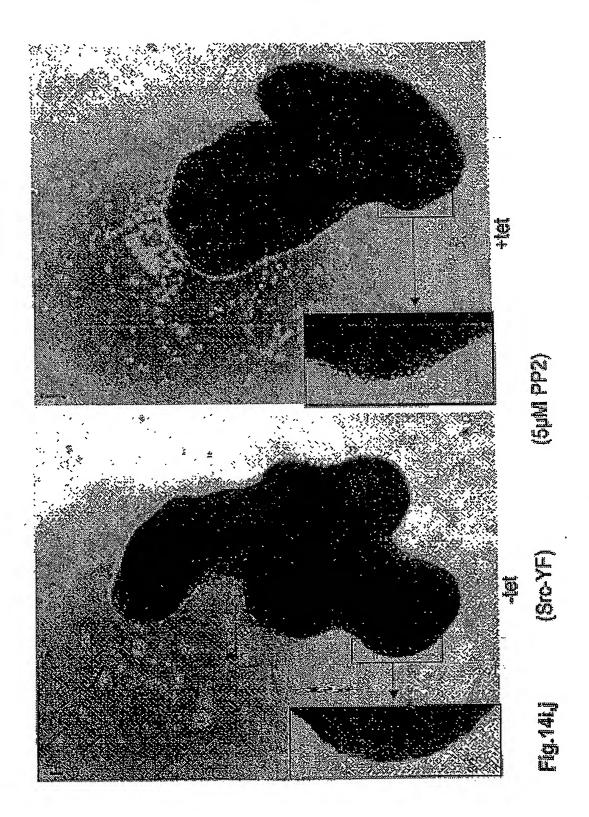


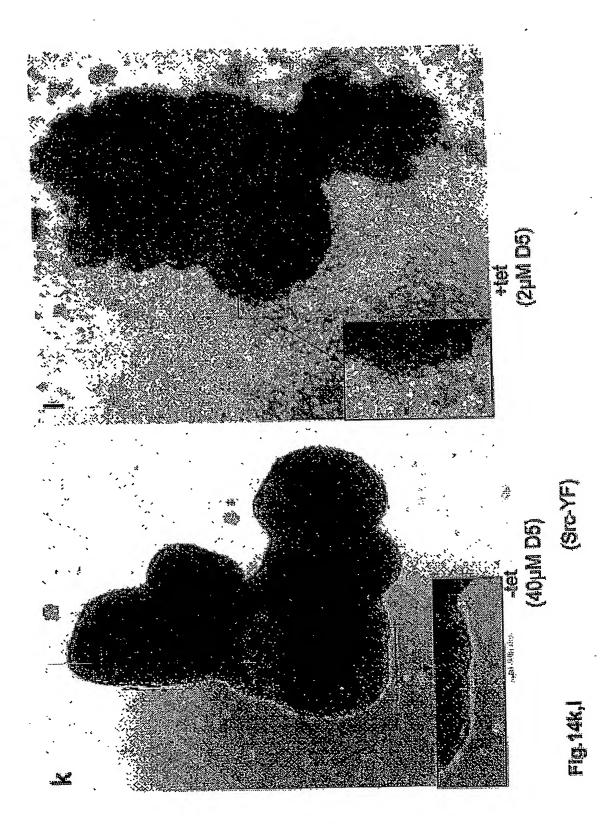


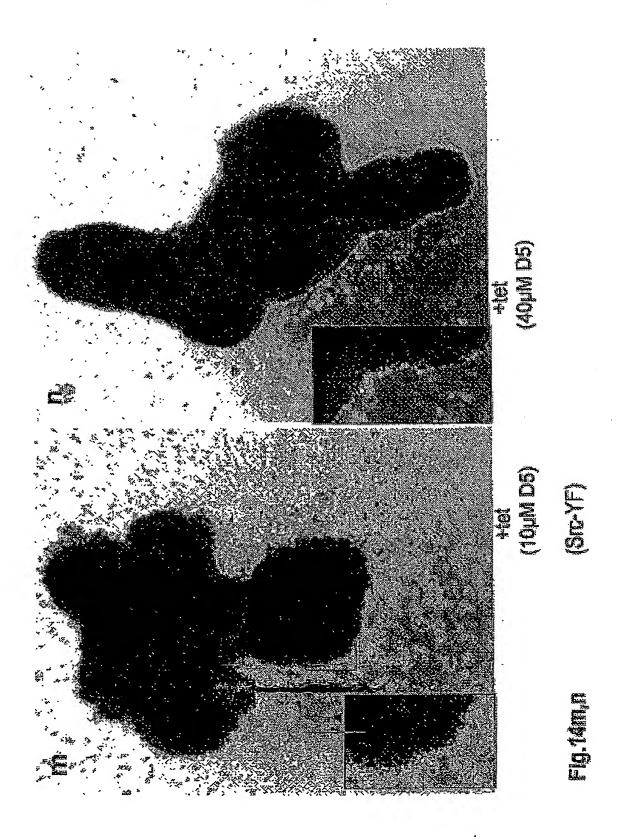




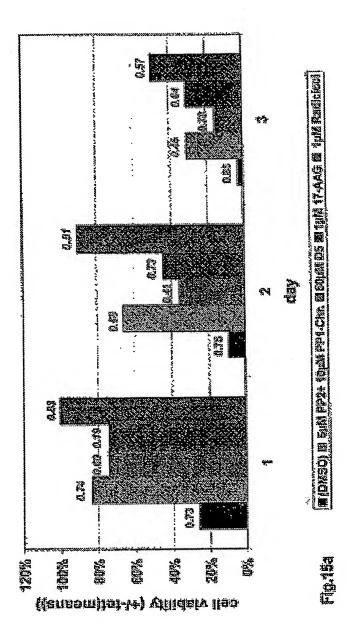






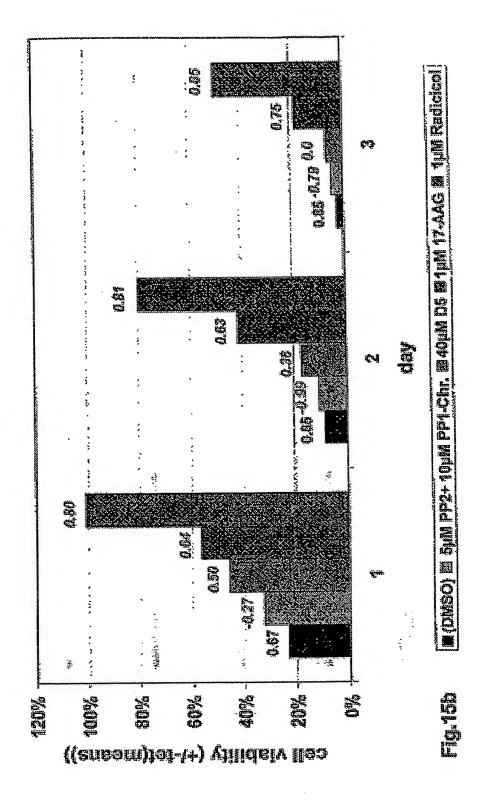


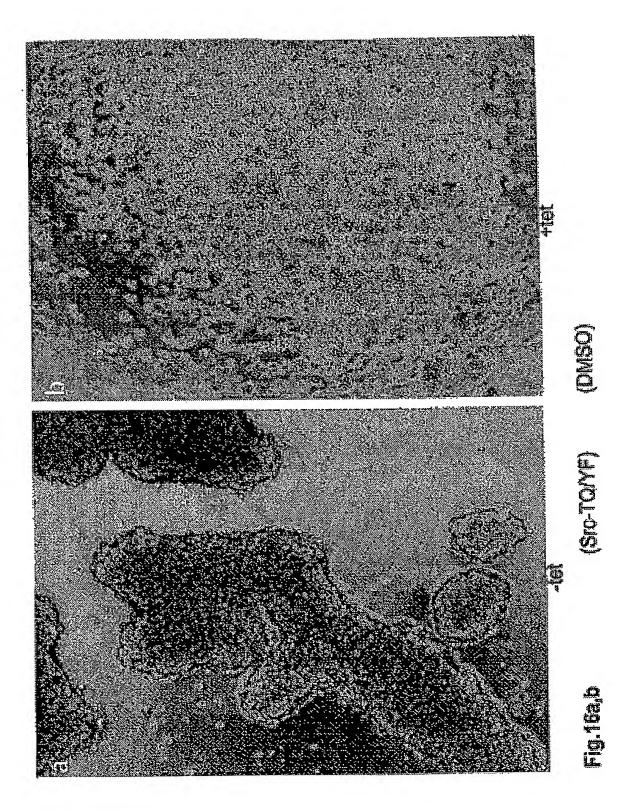


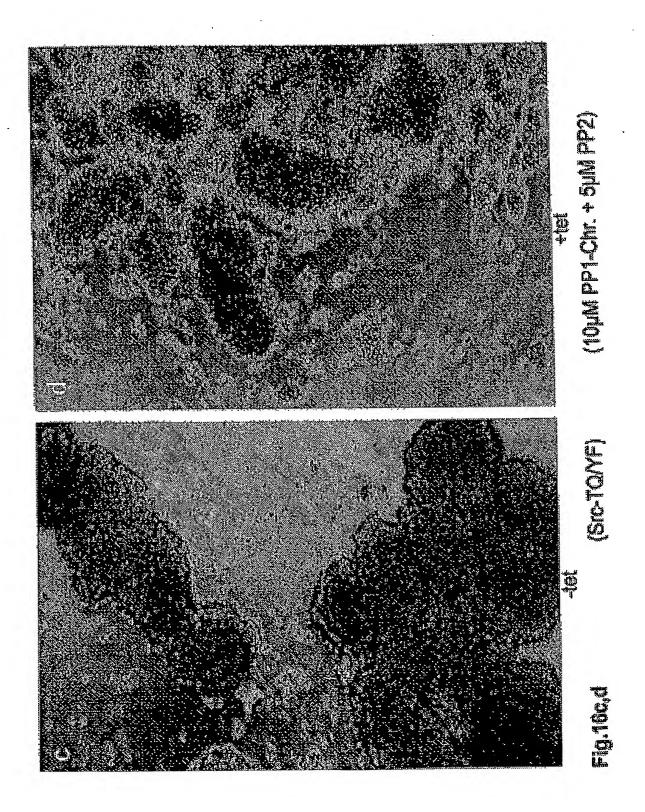


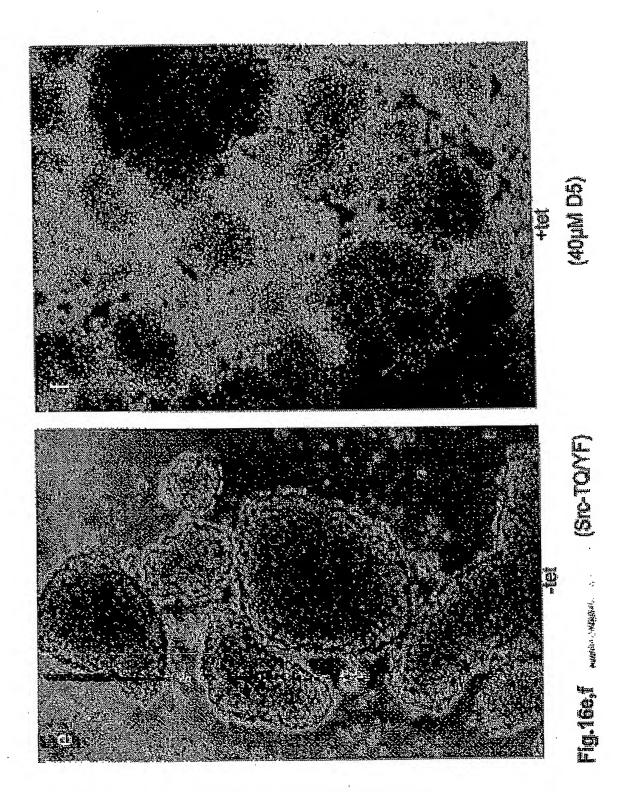
17.

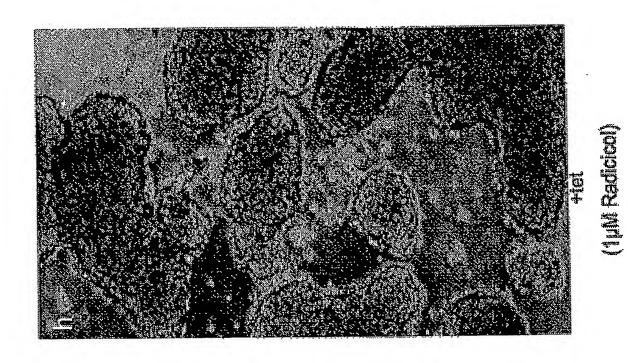
ZM170.24 (CTB)

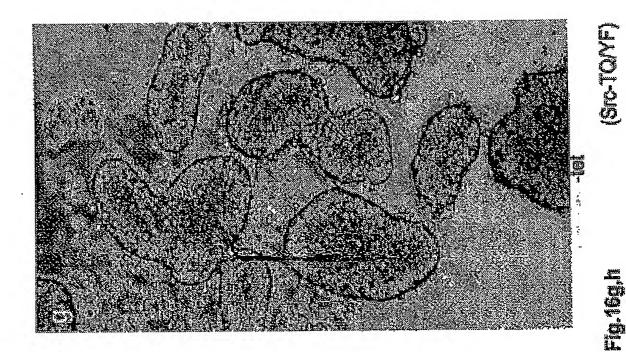


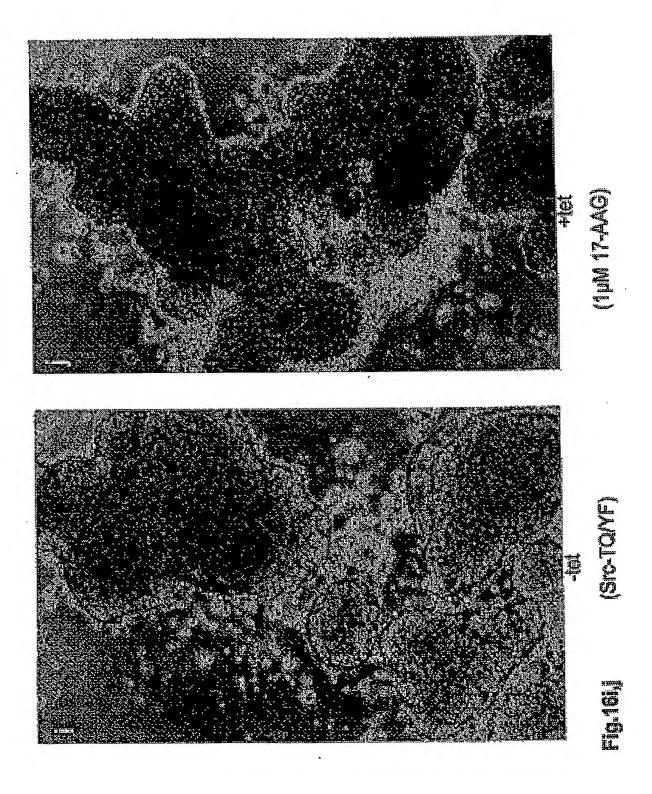


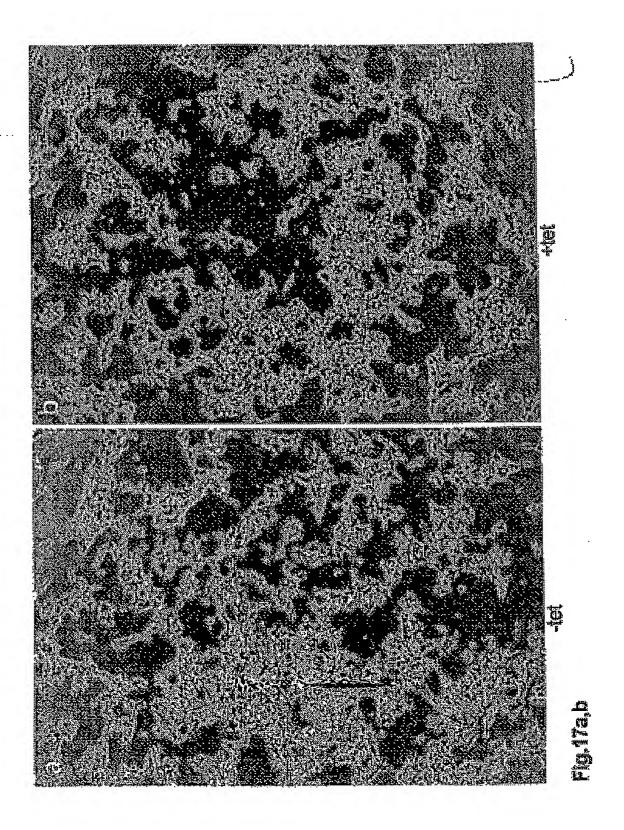












52/63

(1)

Src	U
Yes	MGCIKSKENKSPAIKYRPENTPEPVSTSVSHYGAEPTTVS
=	ATKLTEERDGSLNQS-SGYRYGTD
Fyn Yrk	SGKGQGGSGTGTPAH-PPSQYDPD
	MGCVNOKHKI SONOZODO ZODO ZODO ZODO ZODO ZODO ZODO ZO
Fgr	GGRSSCEDPGCPRDEERAPRMGCMKSKFLQVGGNTFSKTETSASPHCPVYVPDPT
Hck	GGRSSCEDPGCPRDEERAPRINGCMKSKF LOVIGEN TSKILLISASI ICE VIVELI
Lyn	MGCIKSKGKDSLSDDGVDLKTQPVRNTERTIYVRDPT
Lck	WMENIDVCENCHYPIVPLDGK
B1k	IKEKDKGQWSPLKVSAQDKD
	**
Src	PSKPAŠADGHRGPSAAFAPAAAERKLEGGENSSDTVTSPORAGPLAGGVTTFVALY
Yes	PCPSSSAKGTAVNFSSLSMTPFGGSSGVTPFGGASSSFSVVPSSYPAGLTGGVTIFVALY
Fyn	PTPOHYPSFGVTSIPNYNNFHAAGGQGLTVFGGVNSSSHTGTLRTRGGTGVTLFVALY
Yrk	PTQLSGAFTHIPDFNNFHAAAVSPPVPFSGPGFYPCNTLQAHSSITGGGVTLFIALY
Fgr	PTKARPAS-SFAHIPNYSNFSSQAINPGFLDSGTIRGVSGIGVTLFIALY
Hck	STIKPGPNSHNSNTPGIREAGSEDIIVVALY
Lyn	SNKQQRPVPESQLLPGQRFQTKDPEEQGDIVVALY
Lyn Lck	GTLLIRNGSEVRDPLVTYEGSNPPASPLQDNLVIALH
-	APPLPPLVVFNHLTPPPPDEHLDEDKHFVVALY
Blk	APPEPPLVVFNALIPPEPDENDEDK
	SH3
Src	DYESRTETDISFKKGERLQIVNNTEGDWWLAHSLSTGOTGY1PSNYVAPSDS1QAEEWYF
Yes	DYEARTTEDLSFKKGERFOIINNTEGDWWEARSIATGKNGYIPSNYVAPADSIQAEEWYF
Fyn	DYEARTEDDLSFHKGEKFOILNSSEGDWWEARSLTTGETGYIPSNYVAPVDSIQAEEWYF
Yrk	DYEARTEDDLSFOKGEKFHIINNTEGDWWEARSLSSGATGYIPSNYVAPVDSIQAEEWYF
Fgr	DYEARTEDDLTFTKGEKFHILNNTEGDWWEARSLSSGKTGCIPSNYVAPVDSIQAEEWYF
Hck	DYEATHHEDLSFQKGDQMVVLEES-GEWWKARSLATRKEGYIPSNYVARVDSLETEEWFF
Lyn	PYDGIHPDDLSFKKGEKMKVLEEH-GEWWKAKSLLTKKEGFIPSNYVAKLNTLETEEWFF
Lck	SYEPSHDGDLGFEKGEPLRILEQS-GEWWKAQSLTTGQEGFIPFNFVAKANSLEPEPWFF
Blk	DYTAMNDRDLQMLKGEKLQVLKGT-GDWWLARSLVTGREGYVPSNFVARVESLEMERWFF
PIK	* ** : ** : ::: *:* *:* *:* *:* *:* *:*
	SH2
Src	GKITRRESERELLNAENPROTELVRESETTKGAYCLSVSDFDNAKGLNVKHYKIRKLDSG
Yes	GKMGRKDAERLLLNPGNQRGIFLVRESETTKGAYSLSIRDWDEIRGDNVKHYKIRKLDNG
Fyn	GKLGRKDAERQLLSFGNPRGTFLIRESETTKGAYSLSIRDWDDMKGDHVKHYKIRKLDNG
Yrk	GKIGRKDAERQLLCHGNCRGTFLIRESETTKGAYSLSIRDWDEAKGDHVKHYKIRKLDSG
Fgr	GKIGRKDAERQLLSPGNPQGAFLIRESETTKGAYSLSIRDWDQTRGDHVKHYKIRKLDMG
Hck	KGISRKDAEROLLAPGNMLGSFMIRDSETTKGSYSLSVRDYDPRQGDTVKHYKIRTLDNG
Lyn	KDITRKDAEROLLAPGNSAGAFLIRESETLKGSFSLSVRDFDPVHGDVIKHYKIRSLDNG
Lck	KNLSRKDAEROLLAPGNTHGSFLIRESESTAGSFSLSVRDFDQNQGEVVKHYKIRNLDNG
Blk	RSOGRKEAEROLLAPINKAGSFLIRESETNKGAFSLSVKDVT-TQGELIKHYKIRCLDEG
	*::** ** * * * *:*:*: * *: * * * * * *
1.5. /4/2004 200 / 10	
Src	GFYLTSRTOFNSLOOLVAYYSKHADGLCHRLTTVCPTSKPOTOGL - AKDAWETPRESL (
Yes	GYYITTRAQFDTLQKLVKHYTEHADGLCHKLTTVCPTVKPQTQGLAKDAWEIPRESL
Fyn	GYYITTRAQFETLQQLVQHYSERAAGLCCRLVVPCHKGMPRLTDLSVKTKDVWEIPRESL
Yrk	GYYITTRAQFDTIQQLVQHYIERAAGLCCRLAVPCPKGTPKLADLSVKTKDVWEIPRESL
Fgr	GYYITTRVOFNSVQELVQHYMEVNDGLCNLLIAPCTIMKPQTLGLAKDAWEISRSSI
Hck	GFYISPRSTFSTLOELVDHYKKGNDGLCQKLSVPCMSSKPQKPWEKDAWEIPRESL
Lyn	GYYISPRITFPCISDMIKHYQKQADGLCRRLEKACISPKPQKPWDKDAWEIPRESI
Lck	GFYISPRITFPGLHELVRHYTNASDGLCTRLSRPCQTQKPQKPWWEDEWEVPRETL
Blk	GYYISPRITFPSLQALVQHYSKKGDGLCQRLTLPCVRPAPQNPWAQDEWEIPRQSL
	*.**. * * * * * * * * * * * * * *

Fig. 18

(2)

variation (C)	aa	RLEVKLGOGCEGEVWMGTWNGTTRVAIRTLKPGTMSPEAFLQEAQVMKKLRHEKLVQLYA.
Src	(298)	RLEVKLGQGCFGEVWMGTWNGTTKVAIKTLKPGTMMPEAFLQEAQIMKKLRHDKLVPLYA
Yes	(305)	QLIKRLGNGQFGEVWMGTWNGTTKVAIKTLKPGTMSPESFLEEAQIMKKLKHDKLVQLYA
Fyn	(299)	QLLQKLGNGQFGEVWMGTWNGTTKVAVKTLKPGTMSPEAFLEEAQIMKRLRHDKLVQLYA
Yrk	(298)	TLERRLGTGCFGDVWLGTWNGSTKVAVWTLKPGTMSPKAFLEEAQVMKLLRHDKLVQLYA
Fgr	(291) (289)	KLEKKLGAGQFGEVWMATYNKHTKVAVKTMKPGSMSVEAFLAEANVMKTLQHDKLVKLHA
Hck	(275)	KLVKRLGAGQFGEVWMGYYNNSTKVAVKTLKPGTMSVQAFLEEANLMKTLQHDKLVRLYA
Lyn Lck	(273)	KLVERLGAGQFGEVWMGYYNGHTKVAVKSLKQGSMSPDAFLAEANLMKQLQHQRLVRLYA
Blk	(269)	RLVRKLGSGQFGEVWMGYYKNNMKVAIRTLKEGTMSPEAFLGEANMMKALQHERLVRLYA
DIK		* :** * **:** :: : : : : **: * *: * : : * * *: *:
.400		
Src	(341).	VVSE-EPIYIVREYMSKGSLLDFLKGETGKYLRLPQLVDMAAQIASGMAYVERMNYVHRD
Yes	(348)	VVSE-EPIYIVEFMSKGSLLDFLKEGDGKYLKLPQLVDMAAQIADGMAYIERMNYIHRD
Fyn	(342)	VVSE-EPIYIVEEYMNKGSLLDFLKDGEGRALKLPNLVDMAAQVAAGMAYIERMNYIHRD
Yrk	(341)	VVSE-EPIYIVEFMSQGSLLDFLKDGDGRYLKLPQLVDMAAQIAAGMAYIERMNYIHRD
Fgr	(334)	VVSE-EPIYIVEFMCHGSLLDFLKNPEGQDLRLPQLVDMAAQVAEGMAYMERMNYIHRD
Hck	(332)	VVTK-EPIYII EFMAKGSLLDFLKSDEGSKQPLPKLIDFSAQIAEGMAFIEQRNYIHRD
Lyn	(319)	VVTREEPIYII EYMAKGSLLDFLKSDEGGKVLLPKLIDFSAQIAEGMAYIERKNYIHRD VVTQ-EPIYII EYMENGSLVDFLKTPSGIKLTINKLLDMAAQIAEGMAFIEERNYIHRD
Lck	(316)	VVTQ-EPIYITEEYMENGSLVDFLKTPSGIKLTINKLLDMAAQIAEGMAFIEEKNTIHKD VVTK-EPIYIVEEYMARGCLLDFLKTDEGSRLSLPRLIDMSAQIAEGMAYIERMNSIHRD
Blk	(312)	**: *****: * * * * * * * * * * * * * *
		**: ***********************************
		3#1
Src		BRAANILVGENLVCKVADFGLARLIEDNEYTAROGAKFPIKWTAPEAALYGRFTIKSDVW
Yes		LRAANILVGENLVCKIADFGLARLIEDNEYTARQGAKFPIKWTAPEAALYGRFTIKSDVW
Fyn		LRSANILVGNGLICKIADFGLARLIEDNEYTARQGAKFPIKWTAPEAALYGRFTIKSDVW
Yrk		LRAANILVGDNLVCKIADFGLARLIEDNEYTARQGAKFPIKWTAPEAALFGKFTIKSDVW
Fgr		LRAANILVGERLACKIADFGLARLIKDDEYNPCQGSKFPIKWTAPEAALFGRFTIKSDVW
Hck		LRAANILVSASLVCKIADFGLARVIEDNEYTAREGAKFPIKWTAPEAINFGSFTIKSDVW
Lyn		LRAANVLVSESLMCKIADFGLARVIEDNEYTAREGAKFPIKWTAPEAINFGCFTIKSDVW
Lck		LRAANILVSDTLSCKIADFGLARLIEDNEYTAREGAKFPIKWTAPEAINYGTFTIKSDVW LRAANILVSEALCCKIADFGLARIIDS-EYTAQEGAKFPIKWTAPEAIHFGVFTIKADVW
Blk		**:**:** * **:************************
Src		SEGILITELTIKGRVPYPGMVNREVLDOVERGYRMPCPPECPESDHD-LMCQCWRKEPEE
Yes		SFGILQTELVTKGRVPYPGMVNREVLEQVERGYRMPCPQGCPESLHE-LMNLCWKKDPDE
Fyn		SFGILLTELVTKGRVPYPGMNNREVLEQVERGYRMPCPQDCPISLHE-LMIHCWKKDPEE
Yrk		SFGILLTELVTKGRVPYPGMNNREVLEQVERGYRMQCPGGCPPSLHD-VMVQCWKREPEE
Fgr		SFGILLTELITKGRIPYPGMNKREVLEQVEQGYHMPCPPGCPASLYE-AMEQTWRLDPEE
Hck		SFGILLMEIVTYGRIPYPGMSNPEVIRALERGYRMPRPENCPEEIYN-IMMRCWKYRPEE SFGILLYEIVTYGKIPYPGRTNADVMTALSQGYRMPRVENCPDEIYD-IMKMCWKEKAEE
Lyn		SFGILLTEIVTYGKIPYPGRINADVMIALSQGIRMPRVENCPDENID-IMRACWKERPED SFGILLTEIVTHGRIPYPGMTNPEVIQNLERGYRMVRPDNCPEELYQ-LMRLCWKERPED
Lck		SFGILLTEIVIHGRIPIPGMINPEVIQNLERGIRMVRPDNCPELIG-LINKLEWIGKED SFGVLLMEVVTYGRVPYPGMSNPEVIRNLERGYRMPRPDTCPPELYRGVIAECWRSRPEE
Blk		***: * * * * * * * * * * * * * * * * *
~		nnngn ng minggmann gilana lalannan inn ama i ama in ama
Src		RPTFEYLOAFLEDYETSTEPOYOPGENE
Yes	(537)	RPTFEYIQSFLEDYFTATEPQYQPGENL
Fyn	(531)	RPTFEYLQSFLEDYFTATEPOXQPGENL
Yrk	(530)	RPTFEYLQSFLEDYFTATEPQXQPGDNQ ·
Fgr	(523)	RPTFEYLQSFLEDYFTSAEPQQQPGDQT
Hck	(521)	RPTFEYIQSVLDDFYTATESQTQQQP
Lyn	(507)	RPTFDYLQSVLDDFYTATEGOXQQQP
Lck	(505)	RPTFDYLRSVLEDFFTATEGO QPQP
Blk	(501)	RPTFEFLQSVLEDFYTATERQELQP

Cell Line			MTS	3				ATP	
	day1 (1h)da	ay1 (4h)d	lay2 (1h)d	ay2 (4h)	day3 (1h)da	ay3 (4h)	day1	day2	day3
parameters		• • 1	• , ,	• 1					
ZM74.6 (con)					•				
mean(-tet)	0,164	0,540	0,278	0,777	0,317	1,094	214859	361143	582472
mean(+tet)	0,163	0,585	0,279	0,819	0,337	1,140	214907	359070	587691
SD(-tet)	0,032	0,038	0,038	0,044	0,027	0,082	8968	31090	27383
SD(+tet)	0,011	0,036	0,021	0,025	0,026	0,098	7140	11126	30183
+/-tet (means)	99%	109%	100%	105%	107%	104%	100%	99%	101%
Z'	-128,00	-3,93	-176,00	-3,93	-6,95	-10,74	-1005,75	-60,09	-32,09
ZM75.7 (Src)									
mean(-tet)	0,106	0,458	0,148	0,534	0,126	0,586	234509	325403	448831
mean(+tet)	0,132	0,485	0,145	0,497	0,123	0,396	215792	280839	233775
SD(-tet)	0,029	0,052	0,021	0,008	0,025	0,042	14194	23609	
SD(+tet)	0,004	0,006	0,011	0,025	0,013	0,014	10006	6943	1441
+/-tet (means)	124%	106%	. 98%	93%	98%	68%	92%	86%	
Z	-2,81	-5,44	-31,00	-1,68	-37,00	0,12	-2,88	-1,06	0,79
ZM75.7 (low dens.)									
mean(-tet)	0,053	0,254	0,079	· 0,287		0,358	)		265961
mean(+tet)	0,058	0,252	0,075	0,261		0,242			1
SD(-tet)	0,010	0,029	0,004	0,025		0,019		ł	
SD(+tet)	0,013	0,029	0,003	<b>~ 0,004</b>		0,018	12953	L .	i .
+/-tet (means)	1,10%	99%	95%	§ 91%		68%			
<u>Z</u>	-12,80	-86,00	-4,25	2,35	-35,00	0,04	· -3,89	-0,13	0,75
ZM76.3 (Src-KA)									l
mean(-tet)	0,205	0,658	0,374	1,115		1,453		530924	
mean(+tet)	0,279	0,674	0,245	0,803		1,096	1		
SD(-tet)	0,054	0,018	0,041	0,101	0,012	0,108		1	
SD(+tet)	0,067	0,053	0,020	0,1078	0,019	0,102	4554		
+/-tet (means)	136%	103 🎇	65%	<b>₹ 72%</b>	67%	75%	20		1
Z	-3,91	-12,31	-0,42	-0,72	0,26	-0,76	<sup>20</sup> -11,59	-0,01	-0,02
ZM76.3 (low dens.)	l.						٠		
mean(-tet)	0,193	0,504	0,264	0,665		0,981		1	597675
mean(+tet)	0,230	0,528	0,218	0,555		0,836			
SD(-tet)	0,039	0,034	0,032	0,043		0,048			1
SD(+tet)	0,061	0,080	0,032	0,032		0,088			1
+/-tet (means)	119%	105%	83%	83%	)	85%	1.		
Z	<u>-7,11</u>	-13,25	-3,17	-1,05	-2,46	-1,81	<u>ি -3,95</u>	-0,09	-0,38

Fig. 19 – (Table 2)

Sheet 1

Cell Line			MTS	<del></del> -				ATP	
	day1 (1h)day	1 (4h)	day2 (1h)da	ay2 (4h)	day3 (1h)c	lay3 (4h)	day1	day2	day3
parameters									
ZM77.2 (Src-YF)									
mean(-tet)	0,244	0,837	0,411	1,190	0,422	1,354	301566	470629	749300
mean(+tet)	0,187	0,464	0,172	0,373	0,130	0,306	205115	171219	95946
SD(-tet)	0,049	0,147	0,053	0,066	0,021	0,055	8963	23671	115199
SD(+tet)	0,054	0,057	0,009	0,015	0,011	0,014	8915	8522	9223
+/-tet (means)	77%	55%	42%	31%	31%	23%	68%	36%	13%
Z'	-4,42	-0,64	0,22	0,70	0,67	0,80	0,44	0,68	0,43
ZM77.2 (low dens.)	•	•							
mean(-tet)	0,162	0,453	0,233	0,587	0,249	0,714	163222	280873	425838
mean(+tet)	0,098	0,280	0,133	0,260	0,137	0,255	106708	91365	48423
SD(-tet)	0,048	0,082	0,028	0,066	0,034	0,051	5612	12255	20592
SD(+tet)	0,029	0,051	0,036	0,046	0,029	0,019	6547	5533	2887
+/-tet (means)	60%	62%	57%	44%	55%	36%	65%	33%	11%
Z' `	-2,61	-1,31	-0,92	-0,03	-0,69	0,54	0,35	0,72	0,81
ZM77.8 (Src-YF)					+				
mean(-tet)	0,294	1,027	0,479	1,337	0,447	1,583	412584	584915	934867
mean(+tet)	0,284	0,634	0,132	0,290	0,125	0,265	303942	183604	91808
SD(-tet)	0,014	0,061	0,042	0,059	0,042	0,037	14686	34945	24413
SD(+tet)	0,038	0,053	0,008	0,021	0,005	0,014	15481	5598	6186
+/-tet (means)	97%	62%	27%	22%		17%	74%	31%	10%
Z	-14,60	0,13	0,57	0,77	0,56	0,88	0,17	0,70	0,89

Fig. 19 – (Table 2)

**Sheet 2 (Continuation)** 

		-	MTS	1		ATP	
Cell line	compound	day1 (4h)	day2 (4h)	day3 (4h)	day1	day2	day3
	parameters						
M74.6 (con)	(DMSO)					201007	1.4701.00
	mean(-tet)	1,372	2,029	2,010	743351	981937	1473106
	mean(+tet)	1,498	2,187	2,331	739807	976312	1473711
	SD(-tet)	0,047	0,047	0,159	29926	70808	49456 58424
	SD(+tet)	0,060	0,066	0,152	43708	66856	58424 <b>100</b> %
	+/-tet (means)	109%	108%	116%	100%	99%	-533,94
	Z'	-1,55	-1,15	-1,91	-61,33	-72,42	-555,84
ZM77.8 (Sro-YF)	(DM SO)			0.400	704964	1108823	1449098
	mean(-tet)	1,642	2,174	2,198	724364 684408	440505	189867
	mean(+tet)	0,915			44042	30574	29608
	SD(-tet)	0,052			35764	7324	8588
	SD(+tet)	0,158			94%	40%	13%
	+/-tet (means)	56%		1	-4,99	0,83	0,91
	Z'	0,13	0,59	0,95	-4,55	5,55	_,_
	10μM PP1-Chr.	4 500	2,282	1,880	724767	1146635	1369267
	mean(-tet)	1,593 1,768			797267	1012586	59342
	mean(+tet) SD(-tet)	0,101		1		29308	5602
	SD(-tet)	0,101	1	Bi .		93100	539 <sup>-</sup>
	+/-tet (means)	111%	L.	3		88%	439
	7'	-1,33	1	1		-1,74	0,7
	itoxicity	0,03	{		+	-0,03	0,0
	suppression	125%		1		81%	35%
	Z' (suppression) 5µM PP2	0,36		l .	-1,47	0,46	0,9
	mean(-tet)	1,744	2,21	1,990	707571	1124429	141766
	mean(+tet)	1,635			1069818	1026247	62863
	SD(-tet)	0,109		d 0,174	27577	19908	6761
	SD(+tet)	0,075	0,20	0,010	105004		961
	+/-tet (means)	94%			:1:	2.2	. 44
	Z'	-4,00	-1,5				0,7
	toxicity	-0,00					0,0
	suppression	86%					36
	Z' (suppression) 1µM PP2	-0,10	F	İ		U,82	٠.
	mean(-tet)	1,58					133786 44428
	mean(+tet)	1,48					3188
	SD(-tet)	0,07		ممما		1	
	SD(+tet)	0,08			1	58%	مت.
	+/-tet (means)	949				1 :2	
	Z'	-3,8		-}			
	toxicity	0,0 \$ 869			17		
	suppression Z' (suppression)	量 869 -0,1			-12	0,46	
	40μM D5	0,98	5 2,28	2,14	B 702816	946287	12847
	mean(-tet)	1,29					
	mean(+tet)	0,08					
	SD(-tet)	0,08			- 1	1	B .
	SD(+tet)	1329			·		B.
	+/-tet (means)	-0,2					1
	kavialt.	0,4		->	+		
	toxicity	171					
	suppression Z' (suppression)	0,4				B	

Fig. 20 – (Table 3)

Sheet 1

			MTS			ATP	
Cell line	compound	day1 (4h)	day2 (4h)	day3 (4h)	day1	day2	day3
	parameters	, , ,					
ZM75.7 (Src)	(DMSO)						
2017-011 (010)	mean(-tet)	1,016	1,488	2,889	609260	83411	4 1068812
	mean(+tet)	1,210	1,461	0,753	592199	81412	546125
	SD(-tet)	0,044	0,097	0,165	10739	3448	4 12829
	SD(+tet)	0,067	0,027	0,090	47653	1820	d 9138
	+/-tet (means)	119%	98%	26%	97%	98'	1
	7'	-0,72	-12,78		-9,27	-6,9	0,87
	10μM PP1-Chr.	-0,72	12.17	-,	,		
	mean(-tet)	0,949	1,553	2,225	547479	73921	932958
	1 ' '	1,087	1,896		- 601706	84718	
	mean(+tet)	0,081	0,084		1		1
	SD(-tet)	0,051			44549		1
	SD(+tet)	115%			1		1
	+/-tet (means)	1	-0,23	1			1
	<u> </u>	-2,02	-0,04				
	toxicity		1				4
	suppression		13179	1			
	Z' (suppression)	ļ	0,31	0,48	-2,77	-0,	0,5
	5µМ РР2				606982	7744	997338
	mean(-tet)	0,983	•				
	mean(+tet)	1,029		1	1	į .	1
	SD(-tet)	0,039					1
	SD(+tet)	0,099	L .			1	
ĺ	+/-tet (means)	105%				•	i
ļ	Ζ'	-8,00			T	+	-+
]	toxicity		0,1		1	I .	
	suppression		16999	_	1	3€	<b>1</b> ₩.
	Z' (suppression) 1µM PP2		*0,7				, ,,,
	mean(-tet)	0,945	1		1		
	mean(+tet)	1,070					
	SD(-tet)	0,040		1			
	SD(+tet)	0,113		1			1
	+/-tet (means)	113%	1119			1	
	z'	-2,67					
	toxicity		30,1			1 Æ	14 0,0 1% 579
	suppression		735			₹ 88¢	
	Z' (suppression)	-8,49		1 -0,0	-8,6	₽ -O,	28 🕴 0,7
	40µM D5		==	1		- The state of the	*.
	mean(-tet)	0,923	1,49	9 2,96	56832	7994	
	mean(+tet)	1,118	1,36	e 0,72	62696	8020	
	SD(-tet)	0,048	0,10	र्झ 0,118	2989	195	67 6352
	SD(+tet)	0,082	1	2 0,084	4026		
	+/-tet (means)	1219			6 1109	d 10	0% 57°
	Z'	-1,00			2 -2,5	-63	44 0,3
	toxicity		-0,0	-}	+		04 0,1
	suppression		-389	1			
	Z' (suppression)	1	-2,6	1	1	1	1

Fig. 20 – (Table 3)

**Sheet 2 (Continuation)** 

			MTS		-	ATP .	
Cell line	compound	day1 (4h)	day2 (4h)	day3 (4h)	day1	day2	day3
	parameters						
M76.3 (Sro-KA)	(DMSO)						
	mean(-tet)	0,981	1,468	1,960	449055	768114	111452
	mean(+tet)	0,756	1,093	1,766	422727	681683	94274
	SD(-tet)	0,025	0,009	0,008	2423	15534	1676
	SD(+tet)	0,023	0,054	0,129	6628	10225	2404
	+/-tet (means)	77%	74%	90%	94%	89%	85
	Z'	0,36	0,50	-1,12	-0,03	0,11	0,2
	2 10µM PP1-Chr.	, 0,50	0,00	.,	5,55	-,	
		1,134	1,590	2,078	439602	677688	111066
	mean(-tet)	0,670		1,524	443628	659560	97115
	mean(+tet)					10350	3577
	SD(-tet)	0,039			8607	20004	3007
	SD(+tet)	0,034					87
	+/-tet (means)	59%					-0,4
	Z'	0,53			r		0,0
	toxicity	-0,16	i .				19
•	suppression	-78%		B .	1		
	Z' (suppression)	0,11	0,51	-1,27	-0,52	-0,50	-4,1
	5μM PP2			1			
	mean(-tet)	0,903			•		103922
	mean(+tet)	0,645	•		1		84080
	SD(-tet)	0,013	0,031		1		
	SD(+tet)	0,013	0,023		1		. 128
	+/-tet (means)	71%	55%	70%			· 81
	Z'	0,70	0,75	-0,46	-1,97		0,
	toxicity	0,08	0,02	0,06	0,01	0,13	
	suppression	-25%	-77%	-198%	4%	-20%	-24
	Z' (suppression) 1µM PP2	-1,01	0,19	-1,70	-63,47	-2,50	-1,
	mean(-tet)	1,073	1,787	2,093	439927	673524	10473
	mean(+tet)	0,706		1	l .	621696	9312
	SD(-tet)	0,136		1	1		317
	SD(+tet)	0,115	l .	1	l .		427
	+/-tet (means)	66%			B .	92%	89
	7'	-1.05	1	1			-0,
	toxicity	-0,09			+	<b></b>	
	suppression	-49%			l .	li .	
	Z' (suppression)	-2,48		1			1
	2 (suppression) 40μM D5	-2,-	0,5	.,	1		. 1
	1 -	0,943	1,46	1,923	408428	728812	10107
	mean(-tet)	0,853	1		1		
	mean(+tet)	0,853	1				
	SD(-tet)	1		1	L		
	SD(+tet)	0,073			1	1	1
	+/-tet (means)	90%		1	1	2	I .
	<u>F</u>	-2,00			+	<del></del>	<del></del>
	toxicity	0,04		1	1	4	
	suppression	58%		1		1	1
	Z' (suppression)	-1,26	-10,3	1 -25,63	-1,09	-0,74	-20,

Fig. 20 – (Table 3)

**Sheet 3 (Continuation)** 

	*		MTS			ATP	
Cell line	compound	day1 (4h)	day2 (4h)	day3 (4h)	day1	day2	day3
•	parameters						
ZM77.8 (Sro-YF)	(DMSO)						
(suspens.)	mean(-tet)				338971	361136	298794
•	mean(+tet)			. '	373161	265548	48428
	SD(-tet)				35198	44643	40668
	SD(+tet)		1		46667	81946	24977
	+/-tet (means)				110%	74%	16%
-	z' `		}	1	-6,18	-2,97	0,2
	10µM PP1-Chr.	1					
٠	mean(-tet)	1			315408	373406	32170
	mean(+tet)				371381	328824	20456
	SD(-tet)		1		21546	40847	4624
	SD(+tet)	ļ			45929	44887	4145
	+/-tet (means)				118%	88%	649
	<b>Z'</b>				-2,62	-4,77	-1,2
	toxicity	I	1		T	-0,03	-0,0
	suppression	1			1	55%	579
	Z' (suppression)	i	1			-6,17	-0,3

Fig. 20. – (Table 3)

**Sheet 4 (Continuation)** 

Cell line	compolind(s)	day1 (1h) d	CTB day1 (1h) day1 (2h) day1 (3h) day1 (4h) day2 (1h) day2 (2h) day2 (3h) day2 (4h) day3 (1h) day3 (2h) day3 (4h)	1y1 (3h)d£	3y1 (4h) d.	ay2 (1h) da	CTB 1y2 (2h) da	ıy2 (3h) da	1y2 (4h)d	ay3 (1h) dɛ́	1y3 (2h) di	ay3 (3h) da		day1	ATP day2	day3
ZM74.6 (con)	(DMSO), mean(+**), SD(-tet) SD(-tet) 	125361 111897 6758 7102 89%	275279 266979 10687 6122 97%	419983 410231 18953 11636 98%	566610 556821 27186 16512 98%	217180 208199 36285 20966 96%	422419 395150 38435 25793 84% -6.07	631629 592766 43142 33652 94%	778296 725569 45047 42062 93%	556718 495674 39737 84729 89% -5.12	996338 953305 43916 77381 96%	1217681 1185588 50249 85363 97%	14129864 13933144 61875 93327 99%	402104 7 400788 7 20220 10504 100%	785223 13 772170 13 40842 32490 98%	330176 352707 89099 53873 102%
ZM77.8 (Src-YF) (DMSQ) mean(-th) mean(-tu) SD(-tet) SD(-tet) +	IDMSO    mean(+lut)   SD(-tet)   SD(-tet)   2	169719 36982 11949 7405 22% 0,56	315671 79192 15146 10158 25% 0,68	458783 115894 21044 12904 25% 0,70	663241 170260 26008 18047 26%	141641 15470 27353 5111 11%	344409 31270 43201 6805 9% <b>0,52</b>	559708 49047 44101 8057 9% 0,69	698350 61403 44432 9092 9% 0,75	522182 1 13357 43140 3743 3% 0,72	1031926 24418 53652 3343 2% 0,83			1	205693 1205693 18363 21047 22% 0,84	15653 51594 15851 8% 0,84
	mean(-tet) mean(-tet) mean(-tet) mean(-tet) SD(-tet) SD(-tet)	89227 69599 37158 9755 78% 78% 6,17 0,47	264473 222334 36389 90.13 84% -2,23 0,16 0,66	407863 341482 32465 9137 84% -0,88 0,71	624029 522177 34161 13873 84% -0,411 0,06 78%	131833 76785 28948 28407 58% -2,13 -0,07	337891 209464 44467 33965 62% 60.83 6.02 6.03 6.32	378766 36275 34207 65% -0,04 62% 0,61	724949 477301 32995 35305 66% 0,17 -0,04 63%	468586 119432 67351 22653 25% 0,23 0,10 0,28	2649580 264874 30228 45182 28% 0,67 0,68 26% 0,40	26096 27223 29% 0,71 0,71 0,43	1445891 444328 70186 31% 0.70 0.06 0.46	516652 10 14802 15535 96% 3,35 -0,17 -0,91	1942 18 385717 (46251 43977 67% 0,19 -0,08 58% 0,57	565831 58299 19961 0.75 -0.12 35%
	mean(+tot) mean(+tot) mean(+tot) mean(+tot) SD(-tet) +/-tet (means) toxicity suppression	121004 82414 8432 6818 6818 69% 0,19 0,29 0,35	261524 189453 11768 11028 72% 0,05 0,17 63%	372068 272646 13479 15432 73% 0,13 0,13 64% 0,57	548258 407763 16475 20243 74% 0,22 0,17 66%	167842 55723 8879 12753 33% 0,42 -0,18	327019 112402 8825 16585 34% 0,64 0,05 0,16	486894 169913 11491 20224 35% 0,70 0,13 0,36	210024 10742 23378 36% 0,73 0,15 0,41	384831 47570 36794 4202 12% 0,64 0,26 10% 0,45	823047 111343 27951 6011 14% 0,20 111% 0,72	1054199 148787 27092 7467 1487 0.89 0.75 0.75	1948233 1948233 2078 9078 15% 0,16 13%	281290 7 388123 4 11408 12431 86% 0,13 0,02 51% 2,14	741950 10 109278 2 34251 34251 55% 0,34 0,34 0,33	029800 298995 37198 6715 0,82 0,26 0,74
	Than 17-AAG Than 1	124362 100683 40292 10651 81% -5,45 0,27 76% 0,34	326686 242705 41781 35603 74% -1,76 -0,03 66%	514368 375968 31727 50988 -0,79 -0,12 64% 0,20	689875 511438 24465 71342 74% -0,61	175357 81625 15080 8765 47% 0,24 40% 0,28	388200 158504 23907 8029 41% 0,58 35% 0,62	575033 244010 30998 12232 42% 0,61 5,03 37% 0,58	696096 308041 35333 13194 44% 0,62 0,00 39% 0,73	288309 79312 38848 21303 28% 0,14 0,45 0,03	625049 176527 54183 20904 28% 0,50 0,39 27% 0,57	801619 224969 27264 24543 28% 0,57 0,57 0,61	9600354 2946973 65559 30306 31% 0,57 0,37 0,64	404563 6 23120 11124 92% -2,14 0,09 72%	643362 8 4455203 4 44756 6055 71% 0,19 0,32 63% 0,81	843381 71950 26384 50% 0,29 0,40 0,70
	mean(-tal) mean(-tal) mean(-tal) mean(-tal) SD(-tal) 4/-tet (means) toxicity suppression	86693 117508 33763 7940 136% 3,06 145% 0,49	187116 203091 20192 6330 112% 1262 041 116%	303961 315140 13952 6220 104% 4,41 105% 0,81	415686 418233 12820 5998 101% -21,16 0,37 101%	59614 49859 3703 3574 84% -1.24 0,58 82% 0,60	130910 119701 6849 4832 91% -2,13 0,62 0,79	206433 187323 13566 2530 91% 91% 90% 90%	257547 232674 17877 17877 90% -1,52 0,63 89% 0,91	73524 44913 8629 15490 61% -1,53 0,86 60%	158606 83176 8627 18080 52% -0,06 51% 51%	201771 103696 9760 19998 51% 0.09 0,38	2500403 1241393 13124 16113 50% 0,30 0,84 48% 48%	55958 3 20328 6348 6348 96% 4,09 0,20 85%	390497 3 323721 1 44772 1 83% -0,15 78% 0,76	330481 182376 14808 5685 55% 0,58 51% 0,82

Sheet 1

Fig. 21 – (Table 4)

							СТВ									
Cell Iine	compound(s) parameters	day1 (1h)d	ay1 (2h)di	ay1 (3h)da	ay1 (4h)d	iay1 (1h)day1 (2h)day1 (3h)day1 (4h)day2 (1h)day2 (2h)day2 (3h)day2 (4h)day3 (1h)day3 (2h)day3 (3h)day3 (4h)	ay2 (2h) d	ay2 (3h) de	ıy2 (4h)d	ay3 (1h)d	ay3 (2h)d	1y3 (3h) d	ay3 (4h)	day1	day2	day3
ZM170.21 (Src-TQ/YF) (DMSO)	(DMSO)	06443	105878	281084	373130	ABDOO	47740B	304163	381943	311151	574626	700179	868149	2561664	91829 7	763065
	mean(+tet)	25108	43333	68534	86620	10096	15357	24203	31319	12747	16575	18160	21033 163495 114769	1634951	14769	61177
	SD(-tet)	14986	13977	23174	24423	6403	23293	19918	15220	54092	65011	40093	39498	13257	20506	
	SD(+tet)	2221	2619	5428	7408	2418	1862	2224	2354	3136	1838	2959	3441	4260	9867	9
	+/-tet (means)	79%	23%	24%	23%	15%	%6	%8 8	%	4%	3%	%	7%	64%	23%	8 8
		0,15	9,0	09'0	0,67	0,55	0,53	0,76	, 8,0	0,42	0,64	18,0	2,80	54,5	9/19	3
	5µM PP2+ 10µM PP1-Chr.	,	907	01010	20000	40004		202000	400040	007070	503400	505004	757083	275755	90775	GRESOS
	mean(-tet)	103525	181753	7,15,197	30797	139340	736220	300303	25045	16004	202400	24764	31805	240458	57810	85764
	mean(+tet)	36551	60348	86/14	11/825	51/4	10928	3/242	97744	800	C+777	26700	2000	10487	10074	2000
	SD(-tet)	27439	12548	22216	30801	30188	27936	3936	3426	26382	43032 4248	4828	5097 11243 8893	11243	8893	5371
	(a) (b)	200	7000	3000	230/	<b>9</b>	¥6	4007	10%	, B	Α6%	<b>70</b> ₩	7%	87%	35%	13%
	+-tet (means)	8 6	2 S	0.55 0.55	5.0	2,0	0.57	0.72	0.80	0.29	0.70	0,83	0,88	66,0	0,75	0,72
	forfolk	969	0.03	0.05	0 0	3.02	-0.38	0.0	-0.14	0.12	0.12	0.15	0.13	900	00,0	0.10
	suppression	86	13%	11%	12%	-13%	*	3%	%2	7%	2%	5%	7%	65%	12%	2%
	Z' (suppression)	-2,07	-0,15	-0,36	-0,27	-0,57	-1,14	-,3	66'0-	-2,27	-1,28	-1,37	-0,79	0,26	-0,30	6 1
	40µM 05					•							-	100	10000	5
	mean(-tet)	59025	129809	194684	287404	60324	129829	221207	285984	192612	376851	469539	602212	235657	8388/ 2	280398
	mean(+let)	29053	59415	86858	121795	13158	25129	38482	48913	16581	24922	29246	36825	681803	91500	1766
	SD(-tet)	6367	13785	23997	29607	11555	15742	22790	24871	17644	23636	3008	45094 95/1 /030 4	2840	14611	3801
	SD(+tet)	1000	4004	3000	40/2	20.07	2027	3	1 5	<u> </u>	2000	769	1	886%	7367	17%
	+/-tet (means)	49% 14	46% 0.24	45% 0.23	0.29	22% 0.11	19% 0.48	0.57	0,64	978	%L'0	0,71	0.73	0,37	9,69	0,76
	tovirity	159	0.30	034	0.28	0.12	0.27	0.27	0.25	0.38	0,34	0,33	0.31	0,08	0,22	0,24
	Suppression	28%	29%	27%	29%	88	12%	10%	10%	2%	4%	4%	4%	%89	<b>56%</b>	40%
	Z' (suppression)	-0,65	0,40	0,43	0,50	-2,22	0,21	0,28	0,38	-0,68	0,03	-0,04	0,09	0,65	0,12	0,49
	Tum 17-AAG	86607	464633	246785	338522	48384	112346	203922	265547	174381	337652		554614	2187763	63272 E	58187
	mean(+let)	52975	92697	137973	189477	21180	48672	84604	109775	35172	62288	77249	99869 209366 237658 206287	209366	37658 2	06287
	SD(-tet)	4711	5003	10361	14402	2873	5601	10794	15146	23121	24919		31506	8939	20132	29298
	SD(+tet)	3735	3300	4519	6725	3887	7851	9489	9196	3635	4201		4932	6240	8067	2371
	+/-tet (means)	61%	26%	26%	26%	44%	43%	<b>4</b> % 0	4.0 % 1.0 % 1.0	20%	18% 0.68	18% 0.76	18%	3.84	65%	0.29
	7	5,0		25.5	, ic	25.0	750	200	2 10	777	0.44	0.38	0.36	:	0.26	0.27
	Coxcity	45%	2,5	42%	43%	34%	38%	36%	36%	14%	16%	16%	16%		25%	31%
	a (companion)	25	2 6	0 64	0 64	0 40	0.30	0.52	0.63	0.42	0.70	0.75	0,75	0,58	0,70	0,47
	1 (Suppression)		eo o	5		2	2			!	<u>:</u>					
	mean(-tet)	28978	80479	143848	208040	23984	53813	98255	130630	55854	121609	159530	210961	22281	47011	57076
	mean(+tet)	28089	80037	143521	209902	19193	42280	78683	103955	41478	68851	80182	104325	19614	1 188375 146974	46974
	SD(-tet)	7167	11510	11810	11321	1437	4892	7496	9799	8290	11249	14580	17102	984	13100	15382
	SD(+tet)	3903	4297	5234	6476	3478	5184	5095	5212	2629	6206	3310	4142		3	416
	+/-tet (means)	%16	%66	100%	101%	80%	%62	80%	80%	74%	22%	20%	%64 070	88%	76%	57%
		-36,36	-106,29	-155,37	27,67	2,08	79'1-	56.0	2 lo	, io	200	76.0	75.0	12.0	0.50	0 5
	toxicity	99'0	) (2,0)	6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6 6	9, 6	6,62	2,5	0,00	70'0	73%	55%	767	48%	67%	%69 ************************************	53%
	Suppression	200	8 5 5	8001	9 6	5 5	0.54	0 C	3 6	5.1	0.70	0.84	0.85	0.61	0.72	98
_	C (aupplession)	) ( ) ( ) ( ) ( ) ( ) ( ) ( ) ( ) ( ) (	;		1	:				•	•					

Fig. 21 – (Table 4)

Sheet 2 (Continuation)

							CTB								ATP	
Cell line	compound(s) parameters	day1 (1h)day1 (2h)day1 (3h)day1 (4h)day2 (1h)day2 (2h)day2 (3h)day2 (4h)day3 (1h)day3 (2h)day3 (3h)day3 (4h) day	lay1 (2h) d	ay1 (3h)d	ay1 (4h)	ay2 (1h) da	ıy2 (2h) da	1 <b>y2</b> (3h) de	1y2 (4h)d	ay3 (1h)da	ay3 (2h)d	ay3 (3h)d	ay3 (4h)	_		day3
ZM76.3 (Sro-KA) (DMSO)	(DWSO)															
	mean(-tet)	85137	212690	308486	458769	169271	321225	503254	597969	683004	1043142		1486974	360168 68		1063461
	mean(+tet)	69235	171904	249989	368416	126929	246859	385894	472102	476847	698222		1090515	325855 594		33648
	SD(-tet)	30925	20046	21723	24337	20595	16811	33146	24905	31744	36323		34932	11095 34		35869
	SD(+tet)	6388	4114	9906	12309	11096	13255	14992	21693	44199	43743		63675	10574 20		51583
	+/-tet (means)	81%	81%	81%	80%	75%	77%	<b>4%</b>	79%	%69	<b>67%</b>	71%	73%	73% 90% 86%		%88
	'n	-6,04	-1,05	-0,58	-0,22	-1,25	-0,21	-0,23	-0,11	-0,04	0,30		0,25	-0,89		-2,18
	5µM PP2+ 10µM PP1-Chr.				•				•							
	mean(-tet)	79832	190340	257065	388395	57160	228681	347763	432365	588188	831477	1094312	1240854	371831 687	¥	062793
	mean(+tet)	97140	181653	240280	362068	49822	140714	237636	294570	263333	431770	623112	724438			79441
	SD(-tet)	21736	18270	12104	20245	24161	37166	30095	36350	90316	69044	75797	78046			38929
	SD(+tet)	19999	20695	23341	30656	17624	12135	23020	24228	40625	43153	53809	61947			38788
	+/-tet (means)	122%	<b>82%</b>	83%	93%	87%	62%	%89	%89	45%	25%	27%	28%		85%	73%
		-6,23	-12,48	-5,34	4,80	-16,08	99'0	-0,45	9,32	0,21	0,16	0,17	0,19		- 1	0,18
	toxicity	90'0	0,11	7,0	0,15	0,66	0,29	0,31	0,28	0,15	0,20	0,19	0,17			0,00
	suppression	216%	<b>16%</b>	<b>%99</b>	%99	49%	<b>%99</b> -	-36%	-51%	-79%	45%	48%	-26%			118%
	Z' (suppression)	-1,42	•1,98	-1,90	-1,46	-8,21	-0,85	-2,45	-1,56	9,6	-0,88	.0,98	-0,86 -28,51			-0,76
	1µM Radicicol															
	mean(-tet)	43719	97175	140618	216029	24975	55887	91209	115934	70370	123574	183709	218308	281947 320		96401
	mean(+tet)	38140	82341	117040	179863	29996	55756	81436	100716	69770	114387	161803	188061	248834 256	• •	39832
	SD(-tet)	2241	7876	9628	14489	5338	5577	7953	9735	17210	21438	20612	19603	11981 12		14742
	SD(+tet)	5356	2375	5091	6341	2237	2616	3297	4114	11084	3062	13104	17682	8764 22		10261
	+/-tet (means)	87%	85%	83%	83%	120%	4001	89%	87%	<b>%66</b>	93%	88%	%98	88%		%62
	Ž	-3,09	-1,07	-0,87	O,73	3,53	-186,63	-2,45	-1,73	-140,47	-8,96	-3,62	-2,70	-0,88		-0,33
	toxicity	0,49	0,54	0,54	0,53	0,85	0,83	0,82	0,81	06'0	0,88	98'0	0,85	0,85 0,22 0,54	•	0,75
	suppression	32%	20%	12%	15%	180%	<b>%66</b>	54%	38%	97%	78%	29%	48%	-53%		-74%
	Z' (suppression)	-9,02	-3,68	-7,96	4,7	0,03	-0,15	-0,57	7,72	-1,22	-0,35	-0,99	-1,90	-7,18	- 1	-1,89

Fig. 21 – (Table 4) She

Sheet 3 (Continuation)

Fig. 22

## This Page is Inserted by IFW Indexing and Scanning Operations and is not part of the Official Record.

## **BEST AVAILABLE IMAGES**

Defective images within this document are accurate representations of the original documents submitted by the applicant.

Defects in the images include but are not limited to the items checked:

BLACK BORDERS
☐ IMAGE CUT OFF AT TOP, BOTTOM OR SIDES
☐ FADED TEXT OR DRAWING
☐ BLURRED OR ILLEGIBLE TEXT OR DRAWING
☐ SKEWED/SLANTED IMAGES
☐ COLOR OR BLACK AND WHITE PHOTOGRAPHS
☐ GRAY SCALE DOCUMENTS
LINES OR MARKS ON ORIGINAL DOCUMENT
REFERENCE(S) OR EXHIBIT(S) SUBMITTED ARE POOR QUALITY
OTHER:

## IMAGES ARE BEST AVAILABLE COPY.

As rescanning these documents will not correct the image problems checked, please do not report these problems to the IFW Image Problem Mailbox.